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Section of Pathology.

President—Professor E. H. KETTLE, M.D.

[*January* 19, 1932.]

The Velocity of Lysis and Clumping during *B. typhosus* Immunization in man.

By OLIVER HEATH, M.D.

THE present generally accepted position is that after subcutaneous injection of *B. typhosus* vaccine in man, the earliest specific response demonstrable in the serum by macroscopic titre tests appears somewhere between the seventh and eleventh day. This is in close agreement with the original findings of Leishman and his colleagues (1905), and leaves an apparent latent period of about a week after inoculation. The possible earlier appearance of the O agglutinins after vaccination has not yet been worked out in man.

Two clinical observations are now submitted, in evidence that reactive changes of some importance develop in man several days before the titre rise, followed by

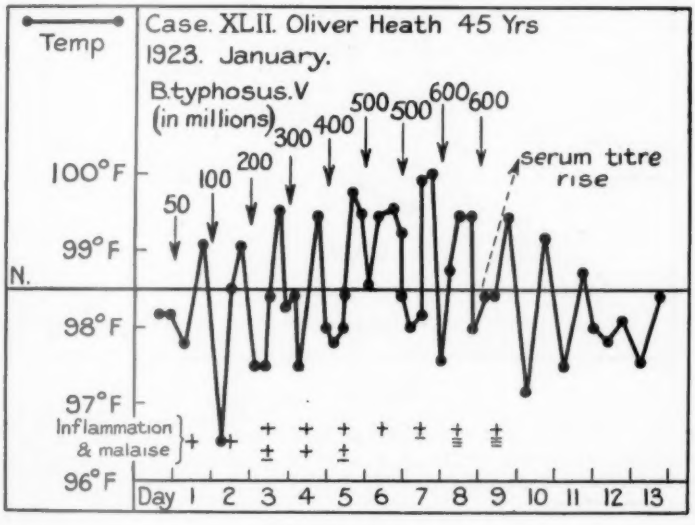


Chart 1.

laboratory experiments planned to discover the nature of this change. The series was completed before research on H and O antigens and antibodies had emerged from the experimental stage, from which it will be clear that ordinary H + O vaccines and cultures were used throughout.

A.—CLINICAL OBSERVATIONS.

Observation 1—*Chart I.*—This experiment with the serum-bactericidal and agglutination details had been previously published by the writer (1924). The present problem concerns the clinical features the fuller analysis of which led on to the work described below.

The subject (O.H.) had last been immunized with 2000 M. *B. typhosus* vaccine rather over two years previously, and still showed low agglutination which, in terms of the Oxford standards, gave a reduced titre (R.T.) of 28, though the serum-bactericidal titre had returned to normal.

Vaccine was prepared by the method of Wright (1921) from a ten-year-old culture of *B. typhosus* (1068), and a series of nine increasing doses injected subcutaneously in different parts of the body on consecutive days.

In the plus-minus line below Chart I, each set indicates the comparative tenderness and duration of the local inflammation, and the associated malaise, following the dose injected on the corresponding day. The earlier reactions were of increasing severity. The fourth was most severe. The fifth showed slight amelioration, while the last four decreased successively to a negligible quantity. The daily temperature curves rose gradually to become continuous on days 5 and 6. From day 6 they again became intermittent and slowly subsided.

It is to be noted that variations in severity of inflammation and malaise preceded changes in temperature by about 24 hours, and that all clinical signs and symptoms

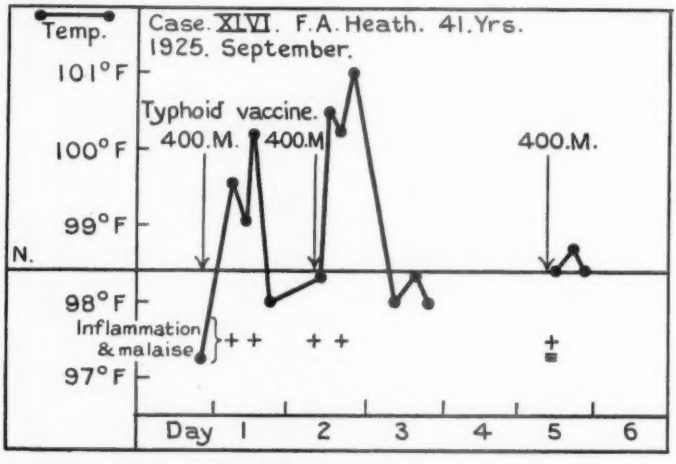


Chart II.

began to abate in the middle of a course of increasing doses of vaccine, three or four days before the first rise of serum titres above their original levels on day 9.

The suggestion is that resistance to the homologous vaccine is increased before the serum titre values.

Observation 2—*Chart II.*—This experiment was planned to confirm and clarify the first, on another subject immunized eleven years previously with two doses of T.A.B. vaccine, but not showing any macroscopic agglutination at the commencement of the experiment. Vaccine was prepared from a five-year-old culture of *B. typhosus* (875).

Two immunizing doses of 400 M. injected on days 1 and 2 each caused fairly severe local inflammation and malaise with rises of temperature to 100° F and 101° F. These reactions were allowed to subside. On day 5, reaction to repetition of the same dose was barely perceptible, and temperature did not exceed 98·8° F. Specific agglutination appeared on day 11 (R.T. = 7).

It is to be noted that power to dispose of (or resistance to) the homologous vaccine, estimated by clinical reaction, is greatly increased on day 5, in this case six days before the titre rise.

Comparing the two experiments, one has to remember that in a subject with normal or low immunity, each single vaccine reaction (gauged by local signs) extends over several days. In experiment I, therefore, each injection after the first was made during the continuance of one or two preceding reactions, thereby having a cumulative effect, and the picture of the experiment becomes a curve. Consequently in experiment I, the 400 M. on day 5, having a cumulative action, caused definite reaction. In contrast to this in experiment II, the 400 M. injected on day 5 when previous reactions had subsided, acted in isolation and the clinical reaction was almost negligible. A similar contrast, seen in one subject within a period of four days, has been previously published by the writer (1924).

Taken together, the variations in clinical reaction indicate clearly that resistance to the homologous vaccine is increased several days before the rise of serum titre values.

B.—Laboratory Experiments.

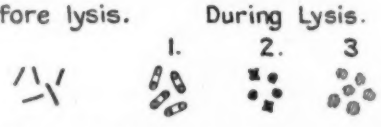
Since it was found impossible to correlate the macroscopical tests with the clinical findings, a series of microscopical observations was undertaken.

I.—*Lysis.*—(1) Technique.—Defibrinated blood (used to facilitate spreading of even films) was mixed in a series of capillary pipettes with equal volumes of 20-hour broth culture, sealed and incubated in a water bath at 37° C. for periods varying from three to thirty minutes, and films prepared and stained by the opsonic method of Wright (1921). Extracellular bacilli were alone noted under a $\frac{1}{12}$ oil-immersion lens.

Diagram 1.

B. typhosus

Changes during Lysis.



Durham (1897) described and pictured the changes seen in the bacilli during lysis. In Diagram I these are represented in order of appearance, though in practice all may often be seen in one microscope field. The arbitrary end-point chosen was the time when the spherulate form 3 is numerous and tending to predominate, admittedly a qualitative and approximate criterion only, but the difference between the effect of normal and immune serum is much greater than the possible error of estimation.

(2) Normal v. immune.—Protocol I shows that the normal lysis time of twenty to twenty-five minutes is reduced by immunization to about six minutes. Further, somewhere within two years after immunization it has returned to normal; intervening tests were not made since duration is only of secondary interest in this communication.

Protocol I.

Subjects	True normals	Immunized			
		1-3 mths.	2 yrs.	5 yrs.	10 yrs.
Number of cases	6	12	O. H.	H. S. W.	F. A. H.
Lysis time	20-25 min.	5-6 min.		20-25 min.	

(3) Early changes after inoculation.—Protocol II records daily estimations before and after immunization of a previously normal subject. Lysis time is slowly reduced between the fourth and seventh day. On day 8 the films showed plainly

that a larger proportion of the bacilli were affected, and on this day the first rise of serum-bactericidal titre was detected.

PROTOCOL II.

Case LIII.—400 M. *B. typh.* V injected day 1.

Day of experiment	0	1	2	3	4	5	6	7	8
Lysis time (minutes)	20	20	20	20	15	12	10	6	6
					Serum bactericidal titre rise...↑				

It appears from these that velocity of serum lysis is increased by immunization, and the change occurs during a period of days immediately preceding the serum titre rise.

II.—*Clumping and motility.*—(1) Technique.—It is essential that the culture be previously replanted daily from broth to broth till highly motile and agglutinable, and be used twenty to twenty-two hours old. It is convenient to dilute with broth to the point where the test serum causes formation of small clumps of ten to twenty bacilli.

The serums were heated at 56° C. for fifteen minutes, and used undiluted except by culture.

By aid of a teat and capillary pipette equal volumes of serum and culture were mixed on a coverslip, which was picked up on a plasticene ring fixed to glass slide and inverted, then examined as a hanging drop on an electric warm stage at 37° C. under a sixth objective. For comparisons, two preparations were made on one slide at an interval of one minute, and watched alternately.

(2) Normal v. immune.—As shown in Protocol III, some normal serums cause

PROTOCOL III.

			Immunized		
Subjects	True normals		1-3 months	3 years	9 years
No. of cases	7	2	10	O.H.	H.S.W.
Clumping time	10 min.	5 min.	< 1 min.	< 1 min.	
Inhibition of motility	nil	nil	immediate		

clumping in five minutes, others not till ten minutes. Motility is not inhibited within that time. In immunized subjects clumping is evident and motility inhibited before the microscope can be focussed, i.e., within one minute. In contrast to what was noted in relation to lysis, these changes had persisted in two subjects at three and nine years after immunization. Three other subjects showed the same phenomenon persisting with *B. paratyphosus* A and B nine years after T.A.B. vaccine.

(3) Early changes after inoculation.—Protocol IV shows daily records made before and after inoculation of a previously normal subject. The serums were tested separately as collected, and compared serially in couples at the end of the experiment, when the remainder of each was tested for macroscopic agglutination in serum dilutions of 1 in 5 upwards.

PROTOCOL IV.

Case L.—500 M. *B. typh.* V, injected day 1.

Day of experiment	0	1	2	3	4	5	6	7	8
Clumping time (mins.)	10	10	10	10	10	5	5	1	1
Inhibition of motility	0	0	0	0	0	±	+	++	++
					Serum agglutination titre rise.....↑				

The normal clumping time of this subject was ten minutes, and was reduced to five minutes on day 5, with partial inhibition of motility and to under one minute with complete inhibition of motility on day 7, when macroscopic agglutination was present in a serum dilution of 1 in 10 (R.T. = $1\frac{1}{2}$). Of four other true normal subjects, two showed the first time reduction on day 5, and two on day 4. In one

case the change occupied five days, a sudden time reduction on day 5, followed by progressive reductions on days 7, 8 and 9, on which day macroscopic agglutination appeared in a serum dilution of 1 in 6 (R.T. = 1).

Clumping and inhibition of motility therefore show a change similar to that seen in lysis, and covering approximately the same period of time.

III.—Opsonic action.—In the light of the foregoing it will be clear that incubation of an opsonic test will be limited by two factors, lysis and clumping, the time-relations of both of which change during the period under consideration. Further, with fresh serum, lysis will interfere with readings more seriously as immunity develops, while with heated immune serums the ingestion of clumps is unavoidable.

It is not difficult to demonstrate increased phagocytosis with immune serums as against normals, especially when using heated serum, but it is, however, not entirely clear that this is due to pure opsonic action of the serum.

The problem of phagocytosis is somewhat complicated, and it is the writer's intention to treat it separately in a future communication.

Experimental Summary.

Evidence is submitted that after an immunizing dose of *B. typhosus* vaccine in man, there is : (*a*) Clinical evidence of increased resistance to the homologous vaccine, (*b*) microscopical evidence of increasing velocity of serum activity seen in lysis and clumping and inhibition of motility, both covering a period of from three to six days immediately preceding, (*c*) the specific rise in serum titre values.

From this correlation of the serological variations with the clinical manifestations it is tentatively suggested that the serum changes may be, in part at any rate, the cause of the clinical amelioration observed during the same period of time.

Discussion.

Experimental methods.—The two latest authoritative textbooks on technique, brought out under the auspices respectively of the British Medical Research Council (1931) and of the American Society of Clinical Pathologists (1931), devote very little space to microscopical methods in serological work, an omission suggesting that such methods are out of favour, which in fact is confirmed by reference to the general literature on the subject. At the same time they reveal a present-day tendency toward macroscopic titre or plating methods. In this latter class, whether planned to determine the number of bacilli killed by a volume of serum, or the dilution of serum which will produce a given (bactericidal or agglutinating) effect on a standard suspension of bacilli, incubation is for a set period of one hour or longer and note is not taken of the pace at which the observed interaction takes place within that time. The method of estimating lysis used by Leishman (1905) must be included in this group, the criterion of a positive result being that all the bacilli shall have become spherulate and rods be absent after incubation for one hour : the earliest change he noted was on day 7 with ordinary doses, but on day 5 or 6 after smaller doses which suggests a small titre rise earlier than was found with a different technique by the writer (1924). Such methods, and these include Dreyer's standard agglutinating technique, could, however, not show the early changes in velocity of action which can on the other hand be readily seen by continuous or intermittent microscopical examination as in the experiments related above. Titre methods show changes in total power, while the microscope reveals both the character and pace of the antibacterial action of serum.

As a general principle in immunological—as opposed to purely technical—

research, one tries to make the test conditions conform to those which might conceivably occur in the body, and to exclude as far as possible artificial manipulations such as dilution of serum or incubation at other than body temperature. Use of heated serum in clumping tests comes in this category of artificial conditions, and objection may be raised to its use the discussion of which would lead far afield and be too lengthy for the present occasion. It was decided to use heated serum for two reasons, viz.: (*a*) heating causes more definite clumping than is obtained with fresh serum, and (*b*) it preserves the serum in such a way that the results can be confirmed in series at the end of the experiment.

Apart from serum tests, immunity variations have usually been estimated by clearing or protection methods. Recently, however, H. D. Wright (1930) used a killed suspension of *B. coli* to compare the temperature response in rabbits before and after immunization : the injections being intravenous, there were no local manifestations, and the general condition of the animals was not recorded. The method is a clearing test with dead in place of live culture, and on hypothetical grounds there does not seem to be any relevant contra-indication to its use in non-lethal doses in man, while, if injections are subcutaneous, additional clinical information is made available.

Experimental results.—The general literature contains many instances of apparent non-correlation of immunity with demonstrable antibody, and the subject is fully discussed by Topley and Wilson (1929), but references to this discrepancy during the first week of immunization are scarce. H. D. Wright (1927), working with pneumococci in rabbits, found specific increased resistance by clearing tests on day 3, but could not in any case show specific agglutination before day 4, and sometimes not at all. In the complete experiments immunity preceded antibody, as shown by titre tests. On the other hand, Lord and Nesche (1929) state that human serum during pneumonia may show agglutination either before or after it has any protective value in mice.

Immunization appears to be a more rapid process in small animals than in man. Henderson Smith and St. John Brooks (1912), using *B. typhosus* in rabbits, reported the first titre changes on day 5, though some of their protocols suggest that lower dilutions would have shown positive results earlier still. R. R. Armstrong (1925, 1931), using pneumococci, found by protection tests in mice the first rise in rabbits on day 3 or 4, in man on day 5 or 6, agreeing here with Lord and Nesche. With *B. pestis* S. Rowland (1912) found immunity well developed in rats by twenty-four hours after inoculation of a killed vaccine or of nucleoprotein extracted from the bacilli, but does not appear to have tested the specificity of the reaction. These variations in the time relations in different species of animals make it necessary to exercise caution in comparing the reports of different workers.

The paucity of recent microscopical work in serology becomes evident from study of the two latest authoritative textbooks concerned with immunology. Topley and Wilson (1929) indeed point out how little has been added since the early years of this century to our knowledge of what may happen when normal or immune serum is mixed with bacteria in vitro (p. 135), and refer to the unsatisfactory state of our knowledge of bacteriolysis, which they attribute largely to the fact that most workers have noted the death of the bacteria and not the actual process of lysis (p. 169).

The velocity of serum activities has seldom been noted in recent work. Bull (1916) refers to the rapidity of agglutination in immune rabbits in vivo, but did not trace its development. The only record known to the writer of experiments planned to observe the pace of agglutination during the course of immunization was made by W. F. Harvey (1915-16). This observer, working with *B. typhosus* in man, watched mixed serum and culture in capillary tubes at room temperature, and

found that undilute normal serum caused fine particulate clumping seen by a hand-glass in twenty minutes; on day 5, 1 in 4 serum clumped slightly quicker; on day 10 clumping was immediate. Allowing for the superiority of the microscope and incubation at body temperature, the character and sequence of events noted agree closely with the present writer's findings.

Since completion and evaluation of the experiments forming the subject of this paper, the question of H and O antigens and antibodies has been considerably clarified, and one can make certain relevant comparisons of some interest.

J. A. Arkwright (1927) has given a very concise description of the microscopical appearances of clumping with specially prepared O and H serums, which correspond in all details with those seen by the writer when using respectively fresh normal and immune serums. The most striking contrast is that normal clumping occurs without inhibition of motility, an O effect; while the clumping developed by immunization is associated with inhibition of motility, an H effect. Secondly, after immunization, lysis (present experiments) and serum-bactericidal power as found previously by the writer (1924) seem to return to normal somewhere probably within one year; these are O effects. In contrast, the rapid clumping associated with inhibition of motility was noted to persist up to nine years after immunization; these are H effects. Felix and Olitzki (1929) emphasize this grouping of H and O antibodies and quote other workers. This agreement of two entirely different and independent lines of research in separating the same groups would seem to have the value of additional though indirect evidence.

Finally, if increase of velocity of serum action be accepted as a relevant factor, it is possible to visualize the development of immunity to *B. typhosus* in three phases, as follows:—

(1) *Preparation.*—Armstrong (1925) called this the inductive period. Previously Andrewes (1910) had made a comparable observation in the development of antibacterial leucocytosis in rabbits. He found that a tissue reaction consisting of proliferation of marrow cells occurred during the first four days. After four days, newly formed leucocytes were thrown into the circulation leading to a peripheral leucocytosis. From this work it appears highly probable that the first few days are occupied by tissue preparation in areas where antibacterial substances appropriate to the infection are to be produced.

(2) *Acceleration.*—In this period the antibacterial action of serum is accelerated, probably without change of titre value, a statement which so far as the writer is aware is supported only by Harvey and himself.

(3) *Augmentation.*—In this period we see increasing titre values of the well-known specific antibodies.

If, however, the increased velocity as described above is accepted as a factor in the development of immunity to the *B. typhosus* in man, the final change from normal becomes increased total power superadded to increased velocity.

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[*March* 15, 1932.]

Sir Aldo Castellani, K.C.M.G., read a short paper on an amœba which he had discovered living parasitically on cultures of a yeast-like fungus — *Cryptococcus pararoseus* Cast., the vegetative form as well as the cysts being found only on the actual growth of the fungus, in the culture, not on the surface of the medium outside it. Sir Aldo described his procedure for isolating the amœba, and outlined its morphological and physiological characters. The paper summarized four notes on the discovery of this parasitic organism published in full in the *Journal of Tropical Medicine and Hygiene*, 1930-31.

Section of Radiology.

President—Professor J. M. Woodburn Morison, M.D.

[*January* 15, 1932.]

DISCUSSION ON SOME PHYSICAL AND MEDICAL ASPECTS OF X-RAY DOSAGE IN MALIGNANT DISEASE.

The Measurement of Penetrating Radiations in Therapy.

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The problems of dosage constitute an important meeting place for clinician and physicist—sometimes, indeed, "battle ground" rather than "rendezvous." The physicist has normally a limited outlook in respect of malignant disease and it is perhaps fair to compare his attitude in some respects to that of the surgeon. The physicist sees only the primary growth and aims normally at delivering a certain minimum amount of energy at every point within a certain prescribed volume, and no energy, or as little as possible, at any point outside this volume, regarding radiation as a rather more flexible and subtle scalpel. This, although we know quite well that it is inadequate, is our basis at the moment and constitutes the main problem from the physicist's point of view. The dose at any point we might define as the energy absorbed during the irradiation per unit volume in a very small volume surrounding the point considered, remembering that using this definition it by no means follows that the same dose of different radiations will produce the same effect either quantitatively or even qualitatively.

This is a matter for further consideration when we have chosen our standard of dose. The extent to which the same dose of different radiations does fulfil this condition will depend on the precise method adopted to measure the radiations, i.e., the type of apparatus we employ. Any physical effect of the radiations, heating effects, photographic effects, chemical changes as in the pastille, ionization effects as in the employment of the "*r*" unit, either of these may be made the basis of a system of measuring dose and has indeed been so used. It is unnecessary to discuss this matter in detail as the Kienböck method, pastille methods, are familiar to all of you. It is perhaps worth examining in a little more detail the most satisfactory of the methods, namely, that based on ionization in air, as it has supplanted to a great extent all other methods and has been adopted for international use as the Röntgen or "*r*" unit of dose.

This unit depends on the ionization produced in one c.c. of air under normal conditions, the dose being measured by the amount of electricity separated in the air and measured under such conditions as to avoid certain well-known and troublesome errors of such measurements. It is to be observed that the unit here suggested, the international "*r*" unit, relates to the ionization and probably the energy absorbed in the volume of air experimented upon, not incident but absorbed energy. In this sense it is a real unit of dose not, as seems often assumed, a measure of incident energy. It automatically takes account of the varying absorption with different radiations, though whether it does so correctly from a therapeutic standpoint, is a problem of great complexity on which the opinions of those here would be very valuable. There is good evidence that over a wide range

of wave-lengths the absorptions of air and tissues run approximately parallel, that is, tissues are to the physicist merely a particularly interesting type of compressed air. Much evidence of a biological character supports the view that the same dose in "*r*" of different wave-lengths does produce the same biological effects, the wave-length range being even quoted as wide as from Grenz rays to γ rays. Whether this is so in therapy is a subject for discussion. Our knowledge of physics is, it seems to me, insufficient to solve the problem precisely, though experiments and theory suggest that for very hard rays, γ rays and hard X-rays, the effect should be independent of λ but that the effects of softer rays might be greater than the dose in "*r*" would suggest. The reason for this is rather more subtle than sometimes is imagined, the effect being dependent not on the greater absorption of the radiations, as this should be automatically compensated in an ionization unit, but rather the change in fundamental mechanism of absorption from recoil effects to photo-electric effects, the former nearly independent of atomic number and the latter very variable with this quantity and therefore taking account of chemical composition.

The time factor, or time spacing of the radiations is, however, all important and complicates the problem of dosage very considerably, so much so as to make a statement of dose almost useless unless accompanied by a precise statement of the time spacing of the radiation.

The effect is somewhat analogous to the law of blackening of photographic emulsions by light in which, not the product of intensity and time (It), but the product of intensity and a certain power (p) of the time (It^p) is constant. The value of p is however variable, values of $p = 0{\cdot}3$ to $p = 0{\cdot}8$ being found to give about the right result in certain cases.

This time factor probably accounts for much of the apparent discrepancy between results for X and γ rays, since in general the γ rays from say, a 1-gm. Ra. pack have an intensity in r of the order of $\frac{1}{50}$ of that used in deep X-ray therapy. The same effect enters, of course, in the use of very heavy filters to produce penetrating beams. We alter both the time and the quality of radiation in most cases.

There is no doubt, however, that the ionization method has many advantages over its rivals. It offers a definite quantity (actually a quantity of electricity) which can be measured with considerable accuracy (easily 0·1%) involving no subjective difficulties such as are present in the estimating of colours of a pastille where errors of 20% easily occur. It is quick and simple, using modern forms of apparatus (in fact the whole measurement is made and automatically recorded without the operator at all), it possesses much less dependence on external conditions of temperature, humidity, concentrations and times which mar all photographic methods, while the extreme delicacy of measuring apparatus involved in attempts to measure directly heat production by the rays is avoided, and the apparatus is reasonably robust and transportable.

We will therefore assume that for X-rays the ionization unit is accepted, and we agree to state our doses in r units. We may now turn to more directly practical matters and ask whether such a unit is really necessary. Is a statement of kv., current, filter, time distance sufficient, or, since there is no doubt as to the answer, how insufficient? We will, in more senses than one, treat the problem superficially and consider only the radiation falling on the surface of the skin. In series of measurements carried on for some time in r, the variation in output of the same set under supposedly the same conditions is astonishing. We may mention the fact that two tubes of practically identical design run off the same apparatus with all electrical conditions the same showed differences of output of 35%, while very large variations occur during the life of a tube. Thus a Coolidge standard tube showed a falling off of output of approximately 40% just before its "death" by puncture, while a coil apparatus with mechanical rectifier run at 200 kv., 4 ma. 0·5 mm. Cu and 40 cm. for a distance showed variations in output from time to time of 30%.

The constancy of the ionization apparatus was carefully controlled by radium. Records of other coil sets under good laboratory conditions show maximum variations of the order of 30%. Experiments in which the barometric height, temperature and humidity were made simultaneously with the X-ray measurement revealed no definite connection between X-ray output and humidity. These very large variations in output are not shown (in my experience) by constant high tension apparatus of, say, the "Stabilivolt" type, but variations of output of the order $\pm$ 5% are still recorded from time to time. Results of a number of measurements spread over approximately two years were given bearing out this statement. This constancy might be thought to be satisfactory and is probably often sufficient, but subtle accidents will show the necessity for constant standardization. Three examples might be given from the writer's recent experience.

(1) The output of a coil outfit was measured with the set apparently running very satisfactorily. The intensity of X-rays was approximately nil! Careful search after overhaul of the complete set revealed that the lead rubber used in defining the beam had fallen diagonally across the applicator and the rays had therefore to pass through a considerable thickness before reaching the patient.

(2) Again, a constant H. T. apparatus appeared to be running entirely satisfactorily, but measurement showed that the X-ray output was approximately 10% of its normal value. This was eventually traced to the fact that the tube in a Holfelder cannon apparatus had been cleaned and replaced with the target facing away from the aperture. Of course nothing was visible from the outside.

(3) In a third case the output of a set suddenly fell to approximately 60% of its normal value, a phenomenon eventually traced to a milliameter which had been disturbed, and whose readings for a given current had doubled.

There must be many other ways in which the output of an X-ray apparatus may fall very considerably, but such accidents point, in the opinion of the writer, to the absolute necessity for very frequent standardization of the output of X-ray apparatus used in therapy. The ideal is undoubtedly the recording instrument used on every patient, but failing this, measurements should be made every day or two, as otherwise it may be necessary to waste much time and energy repeating treatments incorrectly administered. If we are to take advantage of the improvement which may be effected via the *r* unit, such measurements are essential.

Of course, we solve one problem in terms of another. Do ionization instruments keep constant over large intervals of time? Such evidence as there is suggests that they do so in general; only much larger series of observations than we have at the moment can give the answer authoritatively. The means provided by the makers of testing the constancy of many ionization instruments are certainly insufficient, and large variations are possible, though standard times show no variation.

In the remaining time I would like to say something of the problems of dosage in radium therapy, for it seems that here the problems are in certain respects more difficult, and less progress has been made. If, as for X-ray therapy, we think of the dose as the energy absorbed per c.c., then here, too, we must fundamentally choose a unit of dosage in accordance with this idea.

From a physical point of view, the present method of statement of dose in terms of mg. hrs. or millicuries destroyed is evidently a beginning comparable to the statement of kv., current, etc., in the X-ray case. True, we have now a constant output, and therefore the possibility of accurate repetition, but it seems that much more information is needed on such subjects as the actual distribution of radiation throughout the tissues. An admirable commencement has been made by such workers as Murdoch and Stahel, who have determined the distribution of radiation around radium tubes, and attempted to arrange as uniform as possible an irradiation throughout the volume to be treated. Their unit of dose is the absolute cgs. one of

ergs./c.c., but for reasons which were set forth recently[1] it seems advantageous to attempt to make the measurements in *r* units so as to have the results comparable with those for X-rays. The experiments are somewhat difficult, but the results of considerable value in various fields, e.g., in that of protection. My own measurements suggest that 1 mg. hr. at 1 cm. for radium is equivalent to approximately 9 *r*, and it is possible thus to see the enormous doses (of the order of 25,000 *r*) which are delivered close to a buried container compared to the dose received at more distant places.

The desirability or otherwise of stating, say, the minimum dose throughout the tumour in *r* units is, I suggest, an interesting point for discussion since such a method of statement does at least focus attention on the actual absorption in the tumour rather than the source of radiation. Some other method such as the actual counting of the quanta absorbed is possible and even in some ways desirable, but the ionization method is well established and laboratories all over the world have, at least for X-rays, agreed on the unit to an accuracy of at least 1%, though the present experimental work for radium suggests very much larger discrepancies.

To revert here, too, to the practical methods of physical standardization, in the course of the examination of some hundreds of radium containers, it has been demonstrated very clearly that every container for therapeutic use should be measured separately; block tests are not in general sufficient. The individual tests need not be elaborate or very accurate. An accuracy of 2 to 3% is probably sufficient and very easily attained. When fixing the total amount of radium for purchase a higher accuracy is necessary, but the individual checking may be made less accurately but must be performed. As an example in a block of ten 1-mg. needles, one needle was found having a content 1·98 mg. and a second needle 0·2 mg. These had been purchased and sent out by reputable organizations. Again, for very long needles occasionally employed, the inaccuracy of packing along the length of the needle is sometimes very surprising and such as to preclude any possibility of accurate dosage or even reasonable usage. It is therefore of great importance that, before being put into use, every container be properly tested for these factors.

Old and New Theories with Regard to X-ray Dosage in Cancer.

By F. Hernaman-Johnson, M.D.

X-rays, in their earliest application to malignant disease, were of necessity given empirically. Small doses were the rule; this was not, however, due to design, but to the limitations of the apparatus available. Basal epitheliomas, among the skin cancers, and carcinoma of the breast were among the earliest new growths treated. In the latter, microscopic examination of remainders showed abundance of fibrous tissue strangling degenerated carcinoma cells; there were also, in most cases, a few malignant cells, apparently undamaged. You will find a description of this kind in a paper read by a pathologist at the British Medical Association meeting in Liverpool in 1912; it might equally well be read to-day.

About this time laboratory workers were very busy pointing out, on the one hand, the selective effect of X-rays upon embryonic cells; and, on the other, the resemblance between such cells and those of malignant growths, which were regarded as "throw-backs" to a primitive type concerned only with multiplication.

From these facts arose the theory of the combined depressant and stimulant action of X-rays—depressant to cancer cells because they were pseudo-embryonic, stimulant to the healthy surroundings, causing a reaction, with fibrous tissue formation and destruction of malignant elements by natural processes.

[1] W. V. Mayneord, *Brit. Journ. of Radiology*, vol. iv, No. 48, Dec. 1931.

It is probable that there are few, even to-day, who do not pay some sort of lip-service to this theory; but if one is to judge by the bulk of current practice and by modern writings it is almost exclusively the first part which is present to the minds of the majority of workers. I say this because one reads that such and such a number of erythema doses must be got into one kind of tumour, and a greater or lesser number into another kind.

Not only temporary, but even permanent damage to surrounding tissues is accepted as a necessary evil, and it is generally held that what cannot be accomplished in a single "full course" cannot be accomplished at all.

Now, I venture to suggest that progress along the lines of the first half of the theory referred to has nearly reached its limits. This is admitted by some advocates of single course methods, whose only hope of improved results is, like that of the surgeons, to get earlier cases. Others pin their faith in apparatus of increasing power; the millennium will be reached with a million volts.

Physicists, we are told, pick up theories and put them down again as a workman does his tools. Would it not then be a good thing if, "without prejudice," as the lawyers say, we tried working with the second half of our twenty years old theory?

There is, in fact, more collateral evidence in favour of indirect, than of direct action. First, there is clinical evidence. Basal epitheliomata, which are true cancers, although they do not metastasize, will disappear without visible reaction under an X-ray dosage so small that to say it is destructive is absurd. Moreover, the same lesions can be caused to heal by zinc ionization or by high-frequency or static sparks, which are purely stimulant in effect. Breast tumours also will often disappear with fractional dosage, which is insufficient to cause even pigmentation of the skin. That they may recur is beside the point; we are at the moment concerned with the mechanism of their disappearance.

Then there is experimental evidence. It has been shown that a tumour which has been given a dose, which, *in vivo*, would normally cause its disappearance, will, if removed within a day or two, grow vigorously in another animal; and further, that if the bed of a transplanted tumour be previously irradiated the tumour is unlikely to take.

Finally, there is the fact that the whole realm of therapeutics furnishes us with no instance of truly direct action. It was originally claimed that the famous "606" directly killed the organism of syphilis. At first a single dose was prescribed; later, a single course. Now, it is recognized that the drug acts only through calling into action powers inherent in the body cells.

At this point I imagine a voice saying, "All very true, but how do you know that massive dosage is not the best way to produce those curative reactions in normal tissues, with which you are so much concerned?" This argument must be dealt with, because it contains an element of truth. Doubtless the massive dose does stir up the normal tissues to attack, and if, in this attack, all the enemies are slain, everything is well. But if, as it so often occurs, there are some malignant cells so resistant that they are merely stunned, the case is hopeless. For against a fresh advance no troops can be mobilized.

Pursuing the military metaphor a little further, it is generally admitted that, in warfare, a situation may arise of so desperate a nature that it may be necessary deliberately to sacrifice an army on the chance of averting disaster. Such "forlorn hopes" are occasionally successful. If they fail, all is lost. Consequently, they are reserved for emergencies in which, owing to lack of time or exhaustion of resources, there would in no circumstances be any chance of striking a further blow.

Analogous situations occur in the case of malignant disease. Late inoperable carcinoma of the larynx, for example. Here the patient's days are obviously few if something drastic is not done, and as the big dose methods show a small percentage of temporary recoveries, they are justifiable.

What I wish to protest against, even though I be but a voice crying in the wilderness, is the application of similar methods in cases which are not desperate when first seen; when, in fact, the normal expectation of life may be months or even years. Against a scheme of treatment by repeated courses of moderate intensity there is, I know, the argument that tumour cells acquire radio-immunity. I would suggest, however, that the facts are capable of a different interpretation. Ultimate failure to respond may equally be due to what, for want of a better term, may be called "staleness" on the part of the surrounding tissues, or if you prefer a phrase, "exhaustion of their power of response."

With the exact details of dosage in various malignant conditions I am not here concerned. What I am contending for is the recognition of certain fundamental truths: That radiations act chiefly as agents for stimulating the resisting powers of the body; that it is impossible by any practicable radiation dosage to ensure in a few days or weeks the death of all cancer cells; that methods of treatment which aim at conserving tissue response are alone sound in principle.

I will conclude with some reference to these principles as they apply to the treatment of patients suffering from cancer of the breast. First of all, as regards pre-operative treatment. I do not suppose that even the greatest enthusiasts for large doses would advocate a quantity sufficient to do permanent damage to healthy tissues before operation. But what of treatment after operation?

It will be admitted, I think, that the problem of breast cancer is, in these days, the problem of metastasis. Are the metastatic deposits already *in situ* when the diagnosis is made? My own investigations lead me to believe that in 80% of all cases the first intimation the patient has of anything wrong is the accidental discovery of a lump while washing. In many instances signs of bone metastases become manifest within a few weeks of the discovery, or may even precede it. In no case, therefore, can we be certain that latent metastases are not already present when first we see the patient.

Where metastasis shows itself months or years later, two possibilities present themselves: The metastases may have been present at the time of diagnosis, and have lain dormant in the interval; or they may be secondary to cancerous nuclei, missed by operation. In the former case, the malignant cells may be almost anywhere in the body; and even in the latter, when we consider the ramifications of the lymphatics, the possible distribution of latent cancer-cells is extremely wide. To kill them all by direct action in a few weeks is surely a hopeless task. In saying this, I do not forget the statistics of Professor Pfahler, who claims that five-year cures are more than doubled, as opposed to those of surgery alone, by a single course carried out by his saturation method. He says that from 46 to 70% of his patients are alive and well after this period, according to the stage at which the diagnosis was made. Whether anyone else can produce better figures I do not know, but even accepting them at their face value, it means, taking into consideration an inevitable proportion of late recurrences, that at least half the operable cases are doomed to die within ten years.

Is it likely that any modification of detail in these big dose methods can materially improve the results? Doubling the voltage, for instance, or extending the length of the course? To me, at least, it seems improbable. Until we cease to think so largely in terms of killing cancer cells, and consider rather the patient who is cancerous, we shall not make further progress.

A woman who has had a single course of radiation combined with operation, or with radium implantation, returns to her home with the odds at least 50% against a permanent cure. We do not fold our hands after a single effort in the case of patients suffering from tubercle or syphilis: why in the cancer case?

It may well be that the final solution does not lie in radiotherapy at all, no matter how applied. But we know that small doses of X-rays combined or alternated

with ultra-violet light will often enable a patient to survive for years, in the face of visible recurrences, and even of bone metastases. Such dosage can act only through stimulating the patient's powers of resistance. But if the treatment is potent against serious invasion, surely it can often turn the scale when the disease is latent, and the deposits small and inactive. It may be that we shall improve our results by the use of certain drugs, working out the appropriate X-ray dosage to use in combination with them. It has been shown experimentally that small systemic doses of copper or magnesium retard the appearance of tar cancer in mice. In the human subject fluorescein has, I have reason to think, a local effect in enhancing the therapeutic action of radiation on diseased mucous surfaces. There are some who assert that the injection of this drug into the circulation previous to ray treatment is of value in lung cancer. This claim should be examined.

Lastly, progress may possibly come from studying the indirect effects as mediated through the ductless glands.

With a view to encouraging discussion, I submit the following intenticnally dogmatic conclusions:—

(1) The limits of advance by single course methods which involve severe local and general reaction have been reached, or nearly reached.

(2) Radiation cures principally by stimulating local and general tissue resistance. To use a dosage so large that permanent damage is done to healthy parts surrounding a tumour is justifiable only in desperate cases.

(3) In the case of breast cancer, results can be improved only by continuous efforts to maintain the patient's resistance against possible metastasis. It is, therefore, particularly important that the initial dosage of radiation should not be of such intensity as to make response to further X-ray treatment impossible.

(4) We ought to face the fact that while further modification technique may improve results, X-ray therapy alone (and this applies equally to radium) may never offer a final solution.

Dosage of X-rays in Malignant Disease.

By N. S. Finzi, M.B.

The main principle in treating any form of malignant disease in any situation is to give a sufficiently large dose to every malignant cell. It matters not whether such cell is one of a large palpable mass, or is a part of a microscopical remnant left behind after operation and requiring so-called "prophylactic treatment."

The tissues surrounding the growth must only receive a certain dose, but the malignant cells may receive more. This certain dose varies with the type of radiation incident on the tumour, but bears a biological relation to the effect of a similar radiation on the skin. It corresponds, in tumours of average radio-sensitiveness, to a dose that produces, after two or three weeks, a sharp erythema, just short of vesication. The radio-sensitiveness of different growths varies, however, so that some require less than the dose mentioned and others more. In the latter case the growth is not curable by radiations unless used as a destructive agent, and, as far as X-rays used without radium are concerned, this seems to be unsuccessful. Without going too deeply into the reasons, it is now agreed by the majority of radiologists that the alliance of the recuperative powers of the body with the depressant effect of the rays on the malignant process should be aimed at.

The rest of the body should receive as small an amount of radiations as possible.

Time factor.—If a dose is applied during the course of a few hours its biological effect is very different from that of the same dose spread over several days or weeks, whether applied continuously or in a number of doses at intervals. As regards the effect on the skin, if the dose is spread over a week, about 150% of the single dose can be given; over two weeks about 200%; over three weeks about 240%; over four weeks about 260% and over six weeks very little more. The biological effect

on the growth does not, however, quite correspond with that on the skin, as regards the time factor, and in some growths, at any rate, notably those whose growth is very slow, increasing the time factor, provided that the dose is correspondingly increased, is an advantage. The optimum time is not yet known, but for many growths better results have been obtained when the treatment is given in four or six weeks than in two or less.

As to the best division of the dose, whether the treatment should be continuous, twice a day, once a day, once every two days, etc., is also not definitely known, but five or six times a week has, in my hands, given good results. It is also possible that an interval in the middle of the course might give better results, but the dose would have to be suitably increased.

Area treated.—The whole area that is likely to be invaded must be treated, particular attention being paid to the possibility of lymphatic spread, though no palpable disease is present.

Homogeneous radiation.—Great care must be taken to get an even distribution of rays throughout this area by cross-fire, distance, filtration, and size of field. One must remember, however, that the deep-seated tumour never seems to receive so large an irradiation as one has calculated. This is evidenced by the biological effect. The reason for it is probably the extra filtration of the tissues causing the deeper parts to receive a harder radiation and, as the hardness of the radiation is increased, so the biological effect becomes less for the same dose and therefore the dose has to be larger. Sometimes an inadequate dose may be increased by the addition of local radium applications.

Wave-length.—It is not possible to specify the optimum wave-length, as a large part of the spectrum has never yet been tried. What we are certain of is that increase of voltage and increase of filtration have, up to 200 kv. and 2·5 mm. of copper, always given us improved results. Further, when similar conditions can be obtained—as, for instance, in rodent ulcer—radium γ-rays seem to be more effective than X-rays.

Dose.—With 200 kv. continuous current and a filter equivalent to 1·5 mm. of Cu, the tumour must receive the biological equivalent of 1,200 roentgens (*r*) given in one dose. Spread over four weeks this therefore becomes 3,120 *r*. This is when it is superficial. If it is deep more must be given, as already explained. In the case of lympho-sarcoma and a few other rapidly-growing tumours, less may be given, sometimes much less. The importance of this is that owing to their rapid dissemination a very large area must usually be treated.

X-rays combined with radium.—(1) Used on the surface, it has been claimed by workers in the Memorial Hospital, New York, that a larger equivalent dose can be given than with each agent used separately. About 65% of an erythema dose of each agent can be given to get the same erythema, a 30% greater dose of the combined radiations than when either is used separately. I have not had much opportunity of testing this, but, using the full erythema dose which we employ at St. Bartholomew's Hospital, I should be wary about trying so full a dose unless worked up to gradually.

(2) X-rays have, in relatively small doses, been used to supplement interstitial radium, dosage being given usually just before the radium has been buried, or after the Ra. needles have been removed. The radium dose should not be much reduced, as the effect of the X-rays is probably to increase the radiation in the spaces between the zones of full irradiation to the amount necessary.

(3) X-rays have been used in full doses either before radium treatment or after. In this case there must be an interval between the two treatments, and I do not think it matters very much which comes first. I have had particularly good results with this method in carcinoma of the cervix, two or three months usually intervening between the treatments.

Factors affecting dosage.—(1) Sepsis: It has been quite definitely shown that, where sepsis is present, the growth is less sensitive to radiations, so that every effort must be made to minimize this before the treatment starts. In many throat cases treatment has failed because the teeth were not properly attended to.

(2) State of patient: If the patient is in a poor condition he will not respond so well to the radiations. In addition, the treatment is a severe strain, and patients always lose weight during it, so that, if the original state of health is bad, the result may be disastrous.

(3) Stage of disease: In nearly every tumour there comes a stage when the growth becomes insensitive to radiations, and this appears to occur whether the patient has been treated by X-rays or not.

(4) Previous treatment: I absolutely disbelieve in the statement which one so frequently sees that one full dose of radiations immunizes the growth against the future action of rays. It is true that a second dose very often has less effect than the first, because of the later stage of the disease and the diminished resistance of the patient, and also because the condition of the skin and subcutaneous tissues often forces one to give a smaller dose. Yet we have patients who have lived many years after a second treatment, and who would not have survived had they not had it.

The time between a full dose and a second treatment must usually be from four to six months at least, and will depend on the condition of the skin and mucous membrane. The second dose will also depend on this, as nearly a full dose as possible must be given.

In some cases one must not refuse a patient the benefit of three, four, or more treatments.

Future of X-ray therapy in malignant disease.—The most important thing at present is to investigate the value of shorter wave-lengths than have so far been used, and this in full doses applied as localized treatments. There are few practitioners in this country who are giving full enough doses of X-rays in malignant disease, and this must be remedied. It needs courage to half kill your patient in order to cure him.

Dr. A. Burrows said that testing radium needles had suggested to him that the ordinary method of distributing the radium in these might be wrong and that a greater intensity at each end might give a better distribution of energy.

Individual nodules of cancer disappeared even if whole tumours did not, showing that there was a bodily mechanism of resistance. As Professor Welsh had suggested, it might be a nice point as to how far, when destroying the supporting tissues of a tumour, on the one hand the tumour cells were being killed, and on the other the natural resistance was being impaired.

A unified biological and physical unit was an impossibility. In consequence, in accurate work he favoured a physical unit. In any case a biological unit was bound, in time, to become a conventional thing which could be expressed then in physical units.

In future, mathematical accuracy in work was essential. Thus, for instance, to work out the problems of the importance of the time factor and intermittence in radiological treatment, it was essential that an accurate unit of measurement should be employed.

Radium provided a steady source of radiation and as such was very valuable in scientific investigations.

Dr. S. Gilbert Scott said that in a document the date of which was probably about 2000 B.C. there was a clear description of the treatment of growths of breast, evidently carcinomatous, by the application of medical pastes, the cautery and other methods, but it was pointed out in this document that, although the original growth might be destroyed by these means, the patient succumbed sooner or later, evidently to secondary deposits.

The agents used to-day were certainly more refined, but the problem of how to prevent or destroy metastases was as yet unsolved, and no efforts were at present being made to tackle this vital question. The radiation of neighbouring groups of lymph-glands—such as those in the neck and axilla, in cases of breast carcinoma—could not influence deposits of secondary growth in the liver. In his (the speaker's) twenty years' experience of malignant disease he had found it rare for the primary growth to destroy the host; metastases of the liver, mediastinum, and spine had accounted for the death of the majority of patients. It was for this reason that about fifteen years ago he had devised the "open" or "dual" method of X-ray therapy, which he still used in addition to any intensive therapy necessary for the primary growth.

Short-wave therapy or the so-called intensive dosage was not applicable in prophylactic treatment, as the pathological cells were situated in unknown positions within the body. Professor Beclere went so far as to state that short-wave intensive therapy should be prohibited in this class of case.

Research work was needed in order to obtain evidence which would decide the question as to whether the destructive effect of radiation on diseased cells was a direct or indirect process; on the answer to this question future developments would depend. As a proof that the direct or killing dose was not the whole story he would show lantern slides [exhibited] from cases of malignant disease treated about twenty years ago. The remarkable results in these cases were obtained at a period when the apparatus used was not capable of delivering a cell-killing dose, and if such results had been obtained to-day they would have been erroneously attributed to the exclusive use of the short-wave therapy. In his (Dr. Scott's) experience the beneficial results from radiation were achieved through some indirect process, and generally best obtained by the use of large fields working within the medium wave-length scale. Control over local manifestations in malignant disease, Hodgkin's disease, leukæmia, etc., would not prevent or destroy metastases.

The great value of radiation as a palliative agent in hopeless cases was not fully appreciated. He would ask the younger generation of radiologists to consider the patient and not to look upon him as an object attached to the tumour.

Professor F. L. Hopwood agreed with Mr. Mayneord that the ionization method of measuring X-rays primarily measured the energy absorbed in the ionization chamber, but since for a given quality of radiation and a given chamber the amount of energy absorbed was proportional to the incident energy in this case, the distinction between incident and absorbed energy need not be stressed. In the case of a tumour, however, until it had been shown that the absorption of X-rays in tissue was proportional to its absorption in a given ionization chamber, measurements made with the latter only gave information of the amount of radiation incident on the tumour and not the "dose" absorbed.

He had found the auto-radiogram method of testing the distribution of radium in needles very satisfactory, provided all needles giving apparent evidence of bad filling were retested before condemnation. It occasionally happened that the abnormal variation in density of the negative was due to a slight cockle in the film or its wrapper, and the repeat test corrected this. There was still doubt as to whether equal amounts of radiant energy of different wave-lengths produced the same biological effects. In the case of a tumour treated by "buried" radium needles, owing to the Compton effect, the quality of the radiation was certainly different from that incident on the same tumour using external radium having the same primary filtration. The dosage in the two cases also appeared to be different.

Reference had been made to the possibility of sensitizing malignant growths to the action of X-rays, by previous painting with fluorescein. He urged that in view of the persistent failure to achieve this result by the introduction of heavy metals, attention should be directed to the converse problem of attempting to *desensitize*

normal tissue to the effects of radiation in order to increase the difference in vulnerability between normal and malignant tissue. The experiments of Dognon on the effect of traces of sodium hyposulphite on the response of some forms of protozoa to X-rays gave a hint that this might be accomplished.

Dr. Claude Gouldesborough said that in his opinion the majority of radiologists were working at the wrong end of the wave-length and the tendency was to work even further in this direction. Dr. S. Monckton Copeman had first brought to his (the speaker's) notice the use of "activated fluorescein" in a case of carcinoma of the male breast, one half of which had been painted with a 2% solution of alkaline sodium fluorescein; the whole tumour had then been irradiated with a dosage of X-rays of moderate penetration (115 kilovolts), with the result that only the painted half responded, and that to a remarkable degree. Professor Lindemann (Professor of Experimental Philosophy at Oxford) had told him that he had been waiting for years for such a method, but expressed surprise that the salt used had had this marked effect on account of the low value of sodium and suggested that potassium and other salts having a higher molecular value should be tried. He, Dr. Gouldesborough, tried potassium fluorescein, but failed to obtain any satisfaction. Professor Lindemann's theory as to the possible action which had taken place was that the fluorescein, having impregnated the tissues and all the tissue cells, was completely inactive until excited or "activated" by the X-rays, when it was induced to throw out a secondary ray, having a photo-chemical action on malignant cells. This ray was probably in that small unknown band about the 500 mark near the ultra-violet line. In this region the rays were of such low penetrative power that they were completely broken up and dissipated by even the minutest layer of air, so that at the present time it was impossible to investigate them. Professor Lindemann, however, did not consider these difficulties to be insuperable, if proper research work could be undertaken. Up to the present, unfortunately, no funds had been available for this purpose or for investigating thoroughly other salts of the fluorescein series. Dr. Copeman and himself (the speaker) were fully aware that the technique was imperfect, but hoped that the work accomplished during the last four years would lead to a great improvement in the future.

Dr. J. E. A. Lynham said that after a good deal of study in the treatment of cases both by radium and by X-rays he had found that one could be sure of obtaining results in certain conditions. Thus, the enlarged spleen found in several diseases could be reduced by doses which appeared to depend on the mass. Enlarged glands of lymphadenoma and even non-caseating tuberculous glands could be caused to disappear. Several non-malignant tumours, such as fibroma or desmoid, could be made to shrink. He had also succeeded in a series of cases of endothelioma in bringing about the disappearance of the tumour by a pre-arranged course of irradiation.

In malignant disease, however, the effect of treatment was less certain, for the response of the tumours appeared to vary, and there was always the possibility of recurrence at a distance. They were much indebted to the physicists for their assistance in obtaining a precision of dosage which was impossible a few years ago. They had been particularly helpful in evolving the rationale of giving a full dose to a deep-seated tumour without causing damage to overlying tissues. Intensive treatment was often necessary to produce the destruction of a malignant growth, but the greatest care should be taken to avoid permanent damage to normal tissues.

When a growth was definitely radio-sensitive it would sometimes respond to radiations of different kinds. Treatment should be kept up after the primary growth had disappeared. Generalized doses of weak intensity, given over large areas of the body, appeared to lessen the number of "takes" in implantation experiments in animals, and might reasonably be expected to reduce the tendency to recurrence.

Dr. Douglas Webster said that there were great variations in the factors of time and intensity. The quickest treatment for malignant disease he knew of was the trial of a curie, in a glass sphere about 0·5 cm. in size, applied at the end of a long rod to a small rodent ulcer for one minute. This had been done in Baltimore. The very shortest treatments he knew of were those of several seconds, a fiftieth of an erythema dose, for sensitive skin conditions, tried in Vienna. These approached "flash" treatments, which might some day be attempted, as "flash" radiography had been tried—but would be hardly as useful!

He had been trying the effect of small treatments in cases of malignant disease, as work by Murphy at the Rockefeller Institute, and by Russ at the Middlesex Hospital, had shown that there was an increased lymphocyte count in animals which had been exposed to small doses of X-rays, and that their immunity to tumour implants had been raised. He (the speaker) had tested this in an advanced case of recurrent breast cancer. He had treated the patient for a supraclavicular recurrence, and had used half a gramme of radium with local success; but there had been further extension of the disease backwards towards the scapula, and infraclavicularly, and there were multiple skin nodules in these areas. Local X-ray treatments were first given for six months and the nodules became flattened; but six months later there were signs of invasion of the opposite breast, and a fresh wider appearance of skin nodules. For this extensive disease the effect of five-minute daily doses, each 15% E.D., was tried, to eight large areas covering the whole trunk. The patient had three courses in all, of this type. A month after the treatment began she "felt much better," and many of the nodules had almost disappeared. Three months after the treatment began, the white count was 9,000, but there was increase of nodules in the scapular region, and the skin was indurated there. Four months later the patient died with chest invasion. The result was inconclusive with such an advanced case, but the general effect appeared to be good; the patient had looked and felt much better.

For large doses in malignant diseases there were many variations in technique, from the one full dose on one day, or divided into several successive days, for X-rays, or for radium, such as the half a gramme of radium (gamma) at 6 cm. distance for twenty-five hours (five or six hours daily), which he had given successfully in some breast cancer cases, to the modifications of Pfahler's "saturation" method, or to Holfelder's and Coutard's X-ray methods of dividing the full dose over three or more weeks. He (Dr. Webster) had himself devised a method after hearing Spear's interesting paper on the radiation of tissue cultures at the Paris Congress. Spear had shown how the irradiation with radium for 2½ minutes, at intervals of 80 minutes, for 1 hour in all, had a lethal effect similar to that of a continued irradiation for 4½ hours. He had tried in a patient with rapidly growing metastases in the neck from tongue cancer the effect of a very divided dose scheme: four irradiations on the first and on the second day, three on the third and fourth days, two on the fifth and sixth, and one on the seventh and eighth, with "saturation" doses on the ninth, and again on the tenth day; the filter was 1 mm. Zn; distance 40 cm. The result had been good so far, and had been followed by shrinkage of the metastatic nodes. These variations as regards the time factor were very interesting. With regard to the intensity factor, Dr. W. M. Levitt referred in his book to the improvement observed with high intensities—as against low intensities—of radiation in cases of breast cancer. He, the speaker, questioned whether Dr. Levitt's observations were soundly based; he himself had observed little or nothing to support such a conclusion. But should Dr. Levitt's judgment on this point be confirmed by future research, it would indicate the advisability of work being done in this country with the 30 ma. deep-therapy type of tube; he believed there was no such tube working in England at present.

Section for the Study of Disease in Children.

President—Sir HENRY GAUVAIN, M.D.

[*January* 22, 1932.]

Right-sided Diaphragmatic Hernia.—REGINALD LIGHTWOOD, M.D. (by permission of Dr. HUGH THURSFIELD).

Male infant, aged 1 year 4 months, one of twins, the other being normal. Has always been thin and is not gaining weight steadily. At the age of four months there was a vomit of altered blood. At six months he had whooping-cough and after this continued to vomit from time to time. Sometimes the vomited material was brown in colour. At one year old, without apparent cause, he had a short convulsive

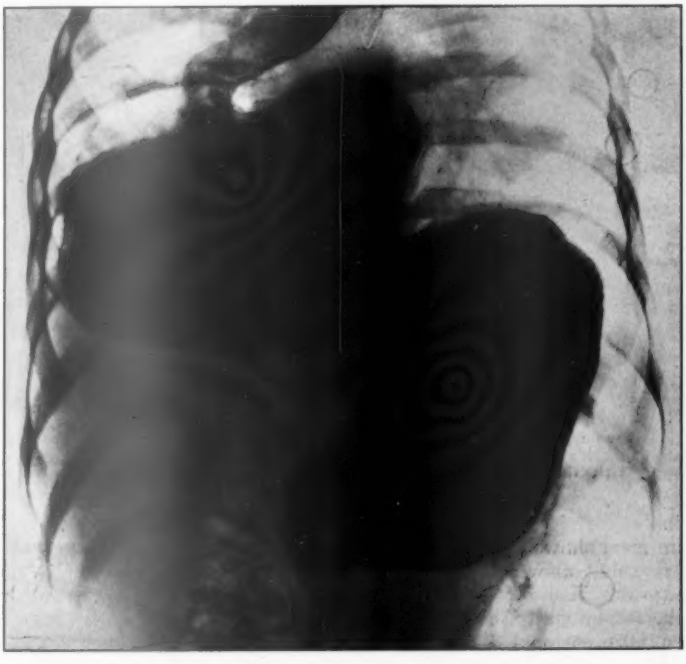


FIG. 1A.—DIAPHRAGMATIC HERNIA.

Barium meal. Time—immediately. Antero-posterior view. The œsophagus is seen at the top of the picture curving to the right to enter the cardiac end of the stomach which lies above the diaphragm. Note the hour-glass constriction of the stomach at the level of the diaphragm.

seizure with cyanosis. A month later was admitted to Guildford Hospital on account of vomiting and general backwardness ; weight then 14 lb.

Examination: A small, pale, rickety baby with square head and open anterior fontanelle, weight 15¼ lb. Physically backward. Does not walk or talk yet. Heart: Displaced to the left with its apex in the fourth space, one finger's breadth outside mid-clavicular line. Lungs: Air entry poor and percussion note impaired at times at right base.

Skiagram of thorax showed heart displaced to left, and shadow to right of mediastinum.

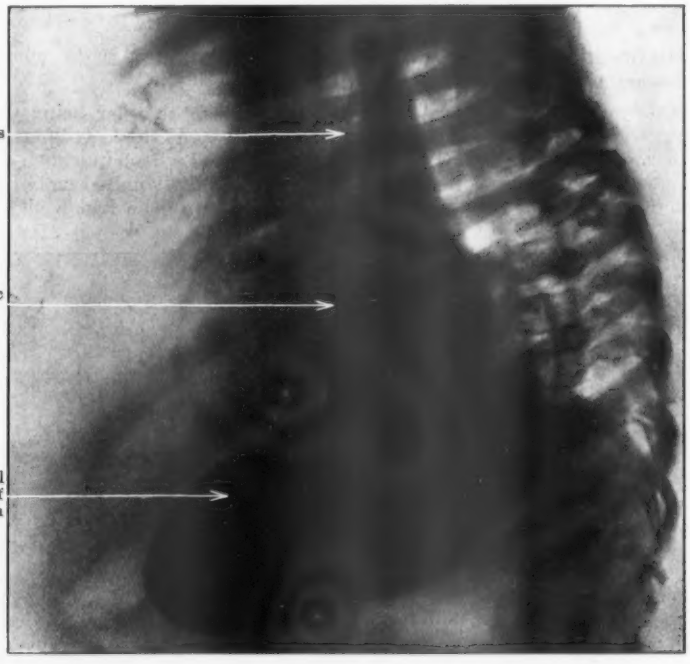


FIG. 1B.—Barium meal. Time immediately. Lateral view. The œsophagus, the intrathoracic portion of the stomach and its abdominal part are filled with barium. Gas-filled colon can be made out on either aspect of the thoracic part of the stomach.

Barium meal showed:—(1) Immediately afterwards—an hour-glass stomach, the upper part being above the right dome of the diaphragm (figs. 1A and 1B); (2) Twenty-four hours afterwards—a loop of colon (hepatic flexure) herniated through the diaphragm to the right of the œsophagus.

In hospital occasional vomiting at night is a feature of the case.

There is a considerable degree of chlorotic anæmia (R.B.C. 5,000,000 per c.mm., Hb. 30%, C.I. 0·3) due to the under-nutrition which has resulted from the diaphragmatic hernia. Wassermann reaction negative; fragility of red blood-corpuscles normal. Direct van den Bergh reaction negative; indirect, slight trace of bilirubin.

FIG. 2,—Barium meal. Time 24 hours.

Antero-posterior view. The colon is partly filled with barium and the hepatic flexure can be traced into the thorax.

Hæmorrhagic Hepatitis : Ætiology unknown.—F. J. POYNTON, M.D., W. W. PAYNE, M.B., and REGINALD LIGHTWOOD, M.D.

Girl, aged 5 years 4 months, second child of healthy parents. Three miscarriages.

Previous history.—Healthy until September, 1931, when she began to complain of sore throat, and was noticed to be thinner. Taken to the Royal Northern Hospital and treated for tonsillitis. No suggestion of hepatic disease at this time.

Present illness.—Two weeks before admission on December 17, 1931, she had a "cold" followed by a cough, and a week before admission jaundice appeared.

Examination.—On admission she resembled an ordinary case of "catarrha jaundice." Afebrile; tonsils inflamed. Liver edge three fingers' breadth below costal margin and extending upwards into fourth intercostal space. Thorax: Signs of pulmonary collapse of portion of right lower lobe.

Course.—Three days after admission she vomited and became suddenly worse. She was frightened and excitable, later drowsy and refusing food. In twenty-four hours she passed into cholæmia and died on December 24 (temperature 104°).

Investigations (made about thirty-six hours before death).—Van den Bergh's reaction: direct, a strong biphasic reaction; indirect, 22 units of bilirubin.

Blood-sugar: 0·200%. Serum calcium, 7·6 mgm. per 100 c.c. Inorganic blood-phosphorus, 2·7 mgm. per 100 c.c.

Plasma proteins: albumin, 3·1%; globulin, 1·7%; fibrinogen, trace.

Wassermann reaction not ascertained for this child, in both parents and in the other child it is negative.

Autopsy.—All the organs, except the brain, bile-stained. Liver: Macroscopically: normal in size (430 grm.), soft, yellow. Careful inspection of its cut surface revealed a fine mottled appearance recalling the pattern of chronic venous congestion of the liver but with the dark areas hæmorrhagic, rather than merely congested. Gall-bladder and bile-ducts normal. Lymphatic nodes in the portal fissure moderately enlarged. Microscopically: Liver cells for the most part destroyed and replaced by diffuse cellular infiltration with polymorphonuclears, lymphocytes and fibroblasts; the few surviving liver cells showed extreme granular degeneration and vacuolation, areas of minute hæmorrhage. A few pseudo-bile canaliculi. Deposits of bile-pigment. Some of the portal radicles showed slight fibrosis, but the bile-ducts were normal. In some areas fine early fibrosis of peri-cellular distribution. Stains for the *Spirochæta pallida* and other organisms, negative. The appearances were those of hæmorrhagic hepatitis with widespread necrosis and slight early fibrosis. Spleen enlarged (80 grm.) and congested. Microscopically it showed only congestion and increased lymphoid activity. Kidneys showed some cloudy swelling of tubular epithelium. Lungs: Areas of collapse in both lower lobes, especially on the right side. Gastro-intestinal tract: Mucous membrane healthy throughout but there was a considerable quantity of altered blood in stomach, small intestine and colon.

Comment.—The chief points are:—(1) The severity and rapidity of the final stage. (2) The completeness of the destruction of the liver. (3) The absence of any apparent cause. (4) The remarkable diminution of fibrinogen.

It is difficult to understand what brought about the sudden transformation of an apparently straightforward case of catarrhal jaundice. No organisms could be found and there was no evidence of syphilis. The early hepatic fibrosis would suggest, however, that the liver had been affected for at least two to three weeks.

The reduction of the fibrinogen supports the experimental observations that the liver is the sole source of fibrinogen. The reduction was so great that no clot was formed in the blood withdrawn for testing, nor were any post-mortem clots found. It is obvious that such a case would be very liable to uncontrollable hæmorrhage. It is possible that the bad reputation of severe jaundice as a cause of hæmorrhage in surgical operations may be in part due to such changes in the fibrinogen content of the plasma.

Pott's Disease of the 4th and 5th Lumbar Vertebræ.—CECIL P. G. WAKELEY, F.R.C.S.

Alfred J., aged 4 years, first complained of pain in his right thigh about three weeks ago; this was followed by inability to stand on his legs after getting up in the morning. His mother noticed a lump in the lower part of the back about two weeks

ago when she was bathing him. He has night sweats occasionally, but eats well and sleeps well.

He is the youngest of eight children, all the rest are healthy and well. No family history of pulmonary or surgical tuberculosis.

On examination.—Definite hard lump over lower lumbar spine; tender on pressure. Fixity of lumbar spine; flexion of spine limited. Skiagrams show

Lateral skiagram of lumbar spine, showing complete destruction of the 5th lumbar vertebra.

complete destruction of body of 5th lumbar vertebra and partial destruction of 4th lumbar vertebra.

Remainder of spinal column quite normal. Small psoas abscess on right side which can be palpated in right iliac fossa.

I am showing this case because I consider that tuberculous disease isolated to the lower part of the lumbar spine is rare in children.

Sclerema Neonatorum.—KENNETH H. TALLERMAN, M.C., M.D.

F. R., aged 10 weeks, was brought to the London Hospital on December 2, 1931, on account of hard lumps which had developed on the forearms one month previously.

Full term infant, normal at birth; instrumental, but not difficult, delivery. Birth weight 9½ lb. Only child. Breast-fed for 2 weeks, then given 4-hourly feedings of a dried milk mixture. General health very good, but had been losing some weight recently.

On examination (2.12.31).—The infant, who was rather poorly nourished, presented a small, hard, raised area the size of a haricot bean, on the right cheek, and one or two similar though larger masses on each forearm. They were oval, with an irregular edge, raised, nodular, and deep to the skin, but apparently attached to it. They did not seem tender, and there was no discoloration.

Admitted to hospital because general nutrition was poor, but while in the ward progressed well and gained weight. No diarrhœa or vomiting. Temperature averaged 99° F. The lesions did not extend but at times appeared rather reddish.

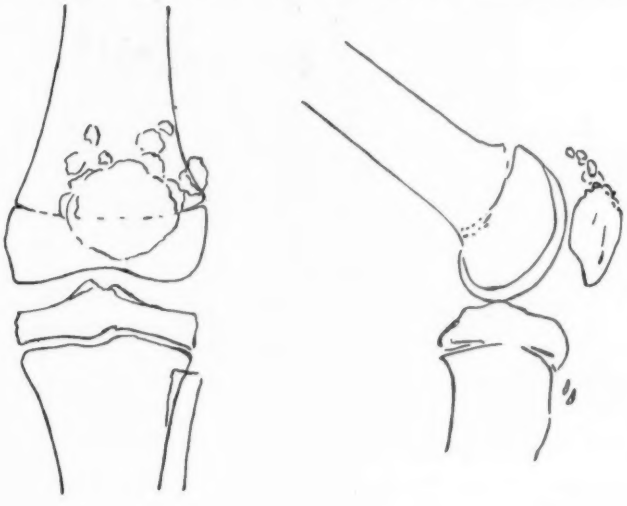
30.12.31: Child doing very well. Lesions on arm decreasing in size, that on face has almost disappeared.

[*February* 26, 1932.]

Enlargement of Patella, of Doubtful Origin.—H. A. T. FAIRBANK, M.S.

W. E. H., a boy aged 12 years.

History.—First seen when aged 3 years and 10 months, on account of knock-knee and flatness of right foot. Right leg noticed to be definitely smaller than left, although equal in length. Condition regarded as mild poliomyelitis. Pes cavus of left foot first noticed early in 1928. Three years ago, in addition to the inequality in



size of legs, and left claw foot, he was found to have a right dorsi-lumbar scoliosis. Knee-jerks plus on right, absent on left. Ankle-jerks both present. Plantar reflex: right, ? flexor; left, not obtained. Abdominal reflexes only obtained in right lower quadrant. There was no equinus and no spasticity. Patient is right handed. Right lower limb remains normal.

He was said to be very nervous; always got a temperature when he was examined at school; often shouted at night; could never be taken to "pictures" and would not sleep in a room alone. Although the left leg had always been larger than the right, the parents only noticed the patella two years ago. The boy is said to have had an attack of synovitis of left knee a year ago.

On examination.—The left patella is apparently enormously enlarged, both in circumference and thickness, being larger than the normal adult bone. The muscles are larger than those of the other leg. Apparently this gives rise to no disability. A skiagram shows that the patella proper, though slightly larger than the opposite bone, is not itself unduly large, the apparent enlargement depending on a number of separate fragments surrounding it above and on the two sides, for a distance as great as three-quarters of an inch. At the insertion of the ligamentum patellæ into the tibia are seen a few fragments of bone not seen in the opposite limb.

The condition seems to call for no treatment.

Gaucher's Disease.—ADOLPHE ABRAHAMS, M.D.

J. C., female aged $4\frac{3}{4}$ years.

History of the condition unknown until four months ago when she first came under observation because of a skin eruption. An enlarged liver and a greatly enlarged spleen were thus discovered. The eruption, which was at first thought to be purpuric, appears to be lichen urticatus and no hæmorrhages have been identified until an epistaxis ten days ago.

The patient was a full-term child, weighing $8\frac{1}{2}$ lb. at birth.

There is no family history of a similar condition; patient has a perfectly healthy brother.

Blood examination.—Hb. 60%, C.I. 0·61. Leucocytes 4,400 with 4% eosinophils and no abnormal cells. Platelets 37,000 to 60,500 per c.mm.

Wassermann reaction, negative. Mantoux test 0·2 c.c. of 1 in 10,000, negative.

Radiologist's report on the long bones: "nothing abnormal."

Report of a section of material obtained from a splenic puncture:—

"The spleen is largely replaced with clear-looking cells of large size in alveolar arrangement. The cytoplasm shows fibrillar structure and in some cases hyaline droplets; a few show diffuse hæmosiderin. Between the alveoli are narrow bands of lymphocytes, polymorphs and some blood. Within the alveoli is slight diffuse hæmorrhage.

Dr. LEONARD FINDLAY: Although one knows that in this disease the mischief is generalized and therefore is not being eradicated by splenectomy this operation at times would seem advisable, and in this case appears to be called for merely because of the size of the spleen extending, as it does, well into the pelvis and beyond the middle line. This line of treatment is supported when we appreciate that there is a degree of anæmia with leucopenia and a diminished number of blood platelets, all evidence of what Dr. Parkes Weber has called hypersplenism.

Regarding the danger of the operation of splenectomy I hold that the risk is not great, both from personal experience and also in view of the number of recorded successes.

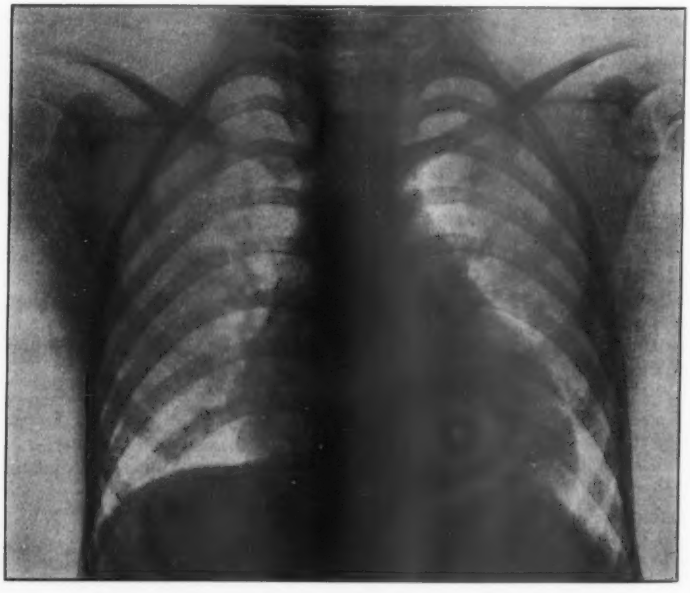
I should consider the use of X-rays in a case like this not only futile but dangerous. X-ray therapy no more than splenectomy can eradicate the mischief but it has the danger of causing severe intoxication from the destruction of protein as was experienced in earlier days with X-ray therapy of leukæmia.

Polycythæmia Anæmica secondary to Congenital Cardiac Septal Defect, in association with an Anæmia-producing Agent.—F. PARKES WEBER, M.D.

The patient, S. S., an English girl, aged 4 years, is known from the age of 2 weeks to have had a congenital defect of the heart. She is the youngest of a family of three children; no relatives are similarly affected. Since her birth she has been subject to occasional periods of slight cyanosis with lassitude, of about two days'

duration ; otherwise she is never cyanosed, but has always had a " bright-coloured " complexion. For the last two years there has been, on and off, a purulent discharge from the left ear, and on February 4 the enlarged tonsils and adenoids were removed by Dr. W. Wilson, to whom I am indebted for the case.

The heart is enlarged on both sides, as may be seen by the radiogram (figure). Over the whole cardiac area is a loud systolic murmur, accompanied by a palpable thrill ; the maximum of both is in the third left intercostal space, close to the sternum. The murmur can likewise be heard at the back of the thorax. Blood-count (February 6, 1932) : Hæmoglobin 60% ; erythrocytes 6,400,000 ; colour-index = 0·45 ; leucocytes 19,400 (basophils 1% ; polymorphonuclear neutrophils 59% ; lymphocytes 28% ; monocytes 9% ; plasma-cells 3%).



Skiagram showing the enlargement on both sides of the heart.

Descriptively I term this blood-picture " polycythæmia anæmica " or " anæmia polycythæmica." Its temporary occurrence in this patient was explained by the presence of polycythæmia rubra as a compensatory reaction towards the congenital cardiac defect (probably an interventricular septal defect), in association with a secondary microcytic anæmia, resulting together with the leucocytosis from the middle ear, tonsillar and adenoid disease. A similar blood-picture of " polycythæmia anæmica " was seen in the woman, with true primary erythræmia (Vaquez-Osler disease), whom I showed on October 9, 1931, at the Clinical Section (*Proceedings*, xxv, p. 10). In that patient the increased number of white cells was due not to a reactive leucocytosis, but was part of her erythræmic (or erythro-leukæmic) syndrome, and the low hæmoglobin value was a result of her delayed recovery from extremely severe hæmatemesis.

On February 20 (two weeks after the above notes were written), when the child's infective condition (tonsils, etc.,) had been removed, and she had been treated by rest in bed and small doses of syrup of iodide of iron, the blood-count was the following: Hæmoglobin 74%; erythrocytes 4,200,000; colour-index = 0·92; leucocytes 9,000 (eosinophils 2%; polymorphonuclear neutrophils 59%; lymphocytes 35%; monocytes 4%).

Bilateral Auricular Fistula.—T. TWISTINGTON HIGGINS, O.B.E., F.R.C.S.

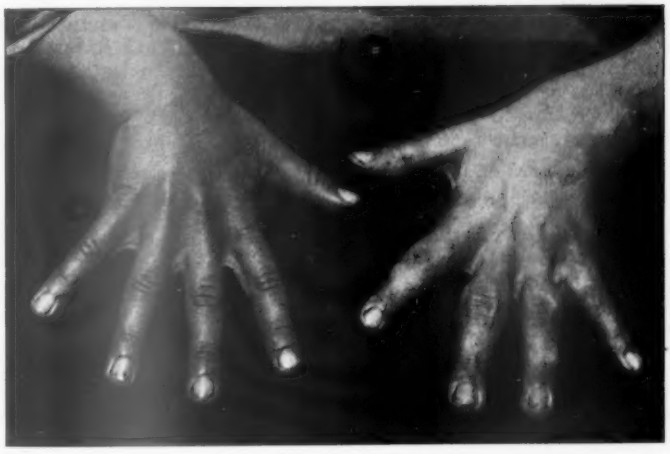
Male, aged 2 years and 5 months.

Symmetrical fistulæ situated at the anterior extremity of the helix at its junction with the tragus. That on the left ear occasionally becomes swollen and discharges.

Father stated to have a similar fistula on one ear only.

Multiple Nævi of the Hand.—T. TWISTINGTON HIGGINS, O.B.E., F.R.C.S.

The patient is a girl aged 6 years, whose left hand is the seat of multiple nævoid growths of unusual character. The growths began two years ago, and are said to have been cauterized at a local hospital. They are fibroid in character, and are situated deeply in the fingers of the hand along the line of the digital nerves in proximity to the finger bones, and here and there in the pulp of the finger tips; in the latter situation the child complains of some pain on pressure; otherwise the growths appear to be painless. One large tumour is situated over the lower end of



the ulna at the wrist. Considerable deformity of the hand has resulted (see fig.). Skiagrams show chronic periosteitis and erosion of the phalanges in places.

One of the growths has been excised, and the section shows "connective tissue with large blood spaces and many groups of nævoid cells scattered throughout," i.e., the appearance is that of a fibrous nævus.

The patient is at present under treatment with radium.

The condition appears to be one of multiple fibrous nævi arising in connection with the periosteum of the finger bones, and to bear some relation to Dr. A. M. H. Gray's case recorded in the *Proceedings*, 1932, xxv, p. 385 (Sect. Derm., 15).

Obesity, ? Nature.—WILFRID SHELDON, M.D.

The patient is a boy, aged 11 years, who has always been chubby but of recent years has grown noticeably fatter. He is an only child of normal parents.

On examination.—The boy is very big. Weight, 17 st. (normal, 5 st.). Height 64 in. (normal 54 in.). The distribution of fat is diffuse, following no particular clinical pattern. The blood-pressure is definitely raised (165/95), but otherwise there are no signs of organic disease. Discs are normal; visual fields show no diminution, skiagram of skull normal. Heart, lungs, abdomen, nervous system: no abnormal signs; urine contained no abnormal constituents. The boy has normal external genitalia, the testes being well developed and completely descended. Secondary sexual characteristics have not yet appeared, and there is no abnormal growth of hair about the body. The voice is rather deep and hoarse. Mentally the boy is quite alert. His appetite is distinctly good, but he is not greedy, and there is no history of persistent overeating.

A blood-sugar curve shows the following figures:—

Fasting blood-sugar	0·078%	During this period the urine contained neither sugar nor acetone
50 grm. of glucose :		
½ hour after, blood-sugar	0·126%	
1 hour after, blood-sugar	0·118%	
1½ hour after, blood-sugar	0·109%	
2 hours after, blood-sugar	0·076%	

I do not regard this case as being typical of any particular endocrine disorder. The distribution of the fat is unlike that associated with dyspituitarism, and there are no localizing signs of pituitary disturbance, such as impairment of the fields of vision or signs of optic atrophy. The raised blood-pressure might suggest that the obesity is possibly related to suprarenal abnormality, but there are none of the other signs usually seen with disorder of the suprarenal cortex. Bigness of build seems to run in the family, as the boy has eight uncles all of whom are policemen, and the most likely explanation of this child's size is that he exemplifies a family characteristic—in his case unusually well marked. If such is the case, one could not expect much from any treatment.

Discussion.—Professor F. S. LANGMEAD said that he had been impressed by the voice of this patient, which was that of an older individual, and the same was true of the mental attitude.

These features, together with the high blood-pressure and the state of the arteries, made him wonder whether there was a suprarenal element in the case.

Dr. LEONARD FINDLAY asked if Dr. Sheldon attached no importance to the systolic blood-pressure of 165. Surely this degree of hypertension removed the case from the class of simple obesity and suggested some endocrine mischief.

At a previous meeting of this Section a tumour of the suprarenal had been suggested as the cause of simple obesity. Was there not in all undoubted examples of a tumour of the suprarenal cortex in childhood, precocious sexual development, as evidenced by the presence of pubic hair or increase in size of the genitalia, both of which features were lacking in this case ?

Congenital Deformity of the Large Arteries.—WILFRID SHELDON, M.D.

Patient, a boy aged 9 years, was examined a year ago by the school medical officer, and was found to have an abnormal heart, for which he was referred to the Rheumatism Clinic at The Hospital for Sick Children, Great Ormond Street. The previous history had been uneventful; there had never been any rheumatic symptoms.

On examination: The boy is fairly well grown and weighs 55 lb. There is no cyanosis and no clubbing of the fingers. The most obvious sign consists of unusually marked pulsation of the arteries on the right side of the neck and along the right clavicle. On palpation in the episternal notch, the enlarged innominate artery can be felt undergoing strong pulsation; the right common carotid and right subclavian

arteries are also enlarged and their impulse is unduly heaving. There is a coarse systolic thrill of maximum intensity in the episternal notch and conducted along the carotid vessels on both sides of the neck. Accompanying the thrill is a systolic bruit of maximum intensity in the episternal notch, but also audible over the whole præcordia, and conducted up the vessels of the neck, along the right subclavian to the right axilla, and posteriorly down the vertebral column to the lumbar region. Pulsation can be felt without difficulty over the abdominal aorta and over the femoral arteries, and serves to distinguish this case from one of coarctation of the aorta. No abnormal collateral circulation. Right pulse bigger than left.

Blood-pressure.—Right arm is 155 systolic; left arm, 125 systolic. The diastolic pressure appears to be the same on both sides and measures approximately 60.

Clinically the heart is not enlarged and its action appears to be normal. A skiagram shows that the heart and aortic shadows are within normal limits.

Other systems show nothing abnormal; urine appears to be normal in amount and colour and is free from albumin.

It is difficult to envisage the precise nature of the deformity in this case. The absence of collateral circulation, together with normal pulsation in the abdominal aorta and femoral arteries, excludes a diagnosis of coarctation of the aorta. Aneurysm, although admittedly rare in childhood, occasionally occurs, but the larger pulse on the affected side and the higher blood-pressure rule out a diagnosis of aneurysm in this case. The presumption which seems to fit the case best is that the innominate artery and its branches are developmentally enlarged—a condition of hæmangiectasia—the enlargement persisting in the right arm at least as far as the wrist, and thus accounting for the larger pulse and higher blood-pressure on that side. Such an explanation, however, offers no reason for the pronounced thrill and systolic murmur heard over the right common carotid and right subclavian arteries.

I wish to thank Dr. Schlesinger for allowing the case to be shown.

Association of Extensive Hæmangiomatous Nævus of the Skin with Cerebral (Meningeal) Hæmangioma.—J. M. ROCKE, M.B., B.S. (for Dr. HELEN MACKAY).

H. S., male, aged 11 months. First child.

History.—Brought to hospital when 3 monhts and 3 weeks old for left-sided fits. Delivered with forceps after mother had been in labour forty-eight hours. Much bruising of head, and a gutter-shaped depression over right parietal bone noticed. Widespread nævoid port-wine staining over head, face and neck at birth. No ill-effects after delivery, and no symptoms for three and a half months when child had first fit. Sudden onset, loss of consciousness and stertorous breathing; left side of face, left arm and left leg twitched. Repeated similar fits occurred; rate of recovery varied.

Seen at Queen's Hospital for Children at this point and admitted.

In hospital.—9.7.31 to 23.7.31: Under observation after onset of fits. 1.10.31 to 15.10.31: For recurrence of fits. 2.11.31 to 5.11.31 and 25.11.31 to 26.12.31: For lumbar puncture after fits. 22.1.32: For repeated fits.

Findings.—Skiagram of skull, normal. Extensive port-wine staining over face, scalp and neck, most marked over left side of face. Increased tone of left arm and leg, which are used less than right.

Eyes.—Movements normal. Occasional nystagmus (to either side) during fits; R. eye larger than L.; R. anterior chamber deeper than L.; R. iris larger than L., and discoloured; R. pupil larger than L.; R. cornea slightly hazy. R.-sided circumcorneal injection. Sclera enlarged but not obviously stretched or thinned. Normal red light reflex obtained in both eyes. Fundi: Left, normal; right optic disc paler and slightly larger. Some cupping on right and (?) increased tortuosity of vessels, suggestive of congenital glaucoma.

Cerebrospinal fluid.—(i) 2.10.31 (twenty-four hours after a fit): Lumbar puncture, fluid under pressure, blood-stained and intimately mixed.

(ii) 6.10.31.—Fluid as above.

(iii) 25.11.31.—Lumbar puncture following fits, fluid clear. Total protein 0·09%; globulin, N.A. and Pandy, negative; cells, 2 lymphocytes per c.mm.; chlorides 0·67%; sugar, no diminution.

(iv) 18.2.32.—Lumbar puncture (20 minutes after fits): Colourless fluid under pressure. Total protein 0·02%; globulin, Pandy, negative; sugar not diminished; chlorides 0·73%; cells, 1 lymphocyte per c.mm.

Dr. F. Parkes Weber reported on a collection of similar cases to the Section of Neurology, December, 1928,[1] and Dr. R. Mackenzie Stewart reported another case in the *Journal of Neurology and Psychopathology*, July, 1931.

Cyanosis probably due to Delay in Evolution of the Blood-forming Mechanism.—W. M. FELDMAN, M.D.

J. F. P., male, 2 months.

Baby was born blue but has become less blue since birth. Dr. Gould states that he saw him five days after birth and that the heart-rate was then 50 beats per minute. After repeated doses of brandy, his heart-rate improved but he lost 1¼ lb. in 10 days, and his breath smelt strongly of acetone.

He is a full-time baby, a "B.B.A.", and weighed 8¾ lb. at birth. The cord was not cut for from 5 to 10 minutes after the baby was born.

The parents are both healthy. The mother was quite healthy during pregnancy; two other children living and healthy, two children dead; one died from heart trouble aged 1 year and 5 months.

Cardiovascular, respiratory, alimentary, and central nervous systems and bones and joints: nothing abnormal discovered. Pulse rate, 40. Spleen not enlarged; liver just palpable. No clubbing of fingers.

Skin deeply cyanosed.

Urine: Acid, faint trace of albumin. No sugar or blood. No evidence of hæmoglobinuria. Deposit: Uric acid crystals numerous. No casts and no pus cells. Gram-negative bacilli (coliform); Gram-positive cocci.

Rectal swab.—Mixed growth of *B. coli* and organisms of the *B. proteus* group. *Wassermann reaction* negative.

	Feb. 1, 1932	Feb. 5	Feb. 8	Feb. 15
Blood counts:				
Red cells	5,520,000	7,336,000	6,990,000	5,760,000
Hæmoglobin %	135%	—	108%	132%
White cells	6,200	14,000	6,200	7,200
Differential:				
Polymorphonuclears	72%	58%	66%	64%
Lymphocytes, small	25%	42%	32%	29%
" large	2%		1%	1%
Large mononuclears	1%	—	1%	5%
Eosinophils	—	—	—	1%
Normoblasts	71,400	114,400	12,600	5,600
Myelocytes	—	7 myelocytes per 100 white cells	—	—

Professor LANGMEAD said he had little doubt that the case was one of congenital heart disease. Some years ago he had carried out a small investigation into the nature of cyanotic cases of congenital heart disease in which no murmur could be heard. He had found that they were examples, as seen post mortem, either of the presence of one ventricle only or of pulmonary atresia. He suggested that this case was due to one of these lesions. There was considerable increase of cardiac dullness to the right.

The blood-picture might be consequent on the deficient oxygen supply, so that normal transition from the fœtal type was retarded.

[1] *Proceedings*, xxii, 431 (Sect. Neuro., 25).

[*The report of other cases shown at this Meeting will be published in the next issue of the* PROCEEDINGS *of the Section.*]

Clinical Section.

President—Mr. CECIL P. G. WAKELEY, F.R.C.S.

[*February* 12, 1932.]

An Enormous Left Renal Tumour.—CECIL P. G. WAKELEY, F.R.C.S. (President).

George P., aged 57, first noticed a lump in the left side of his abdomen in October, 1931: since that date it has increased considerably in size. No pain in abdomen. No history of vomiting. Bowels open daily. Micturition normal.

Since January of this year patient has had intermittent pain in the left sacro-iliac joint; at times this shoots down to the back of the leg. It is most marked at night, when the patient has had a heavy day and has had a good deal of standing. In the leg it is associated with œdema.

On examination.—There is a large stony mass palpable in the abdomen, occupying the whole of the left loin, extending in front just beyond the mid-line, downwards into the left iliac fossa, and upwards to about 2 in. below the left costal margin. Above this level the colon can be felt and percussed. The tumour itself has a smooth outline, and is quite dull on percussion.

The liver is enlarged and reaches almost to the umbilicus and well across to the left side. Its surface is hard, irregular, and nodular. There is no ascites. Hard enlarged glands are present in the left supraclavicular triangle, and in the left groin. Wassermann reaction negative. Blood-urea, 52 mgm. per 100 c.c.

Blood-count.—R.B.C. 2,690,000; Hb. 58%; C.I. 1·09; W.B.C. 15,000. *Differential*: Polys. 86·5%; lymphos. 13·5%.

A barium meal showed nothing abnormal in the alimentary tract. There is no sign of varicocele or œdema of the left leg, in spite of the large size of the renal swelling.

Intravenous pyelography revealed a normal right renal pelvis; nothing could be seen of the left renal tract.

Chromo-cystoscopy showed a normal secretion on the right side; no dye whatever was secreted on the right side. X-ray examination demonstrated a large secondary deposit in the right innominate bone.

It is very uncommon to see a case of hypernephroma of the kidney giving rise to secondary deposits in the glands of the neck and inguinal region.

Old-standing Facial Paralysis treated by Removal of the Inferior Cervical Ganglion of the Sympathetic.—CECIL P. G. WAKELEY, F.R.C.S.

Thomas Mc.C., aged 50, was operated upon for chronic mastoiditis in 1910. During the operation the seventh nerve was severed. Attempts were made to approximate the ends of the nerve three days later, but failed. The patient's main complaint after twenty years of right-sided facial paralysis was that he could not close his right eye and that the eye was always sore and "continually running."

To remedy this, the inferior cervical ganglion of the sympathetic and the first thoracic ganglion were removed through a collar incision in the neck.

The operation was quite easily performed and the eyeball has retracted backwards within the orbit, the pupil is contracted and the upper eyelid falls normally over the globe of the eye, to the entire satisfaction of the patient.

The surface temperature of the right side of the face and arm is two degrees higher than that of the left.

Milroy's Disease.—BERNARD MYERS, C.M.G., M.D.

Miss L. F., aged 47, has suffered from swelling of the right leg from her 20th year; worse after walking, and always worse during hot weather; it does not prevent patient from walking, but putting on her shoes is sometimes difficult. The œdema appears on the foot, especially the dorsum and ankles, and spreads up the leg to the

knee; occasionally it goes to the thigh. No pain or tenderness, but sometimes a pins-and-needles feeling. The power of the leg is good. There has been swelling of the left ankle also. The swelling sometimes becomes acute with headache, and she is convinced that her temperature is then up, although it has not been taken.

Patient has a good appetite; no indigestion but is constipated; menses normal. She is subject to sick headaches; has dyspnœa on swimming or running. Mentally feels very fit; occupation, school teacher.

Suffered from eczema as a child, and measles and jaundice about sixteen years ago; occasionally has nettle-rash.

Her mother suffered from œdema of the legs; a mosquito bite gave rise to a large lump. A sister has irritable palms in the summer.

Patient looks healthy. Heart of normal size; systolic murmur is present, propagated to axilla; pulmonary second sound slightly plus. Blood-pressure: right arm 124/82, left arm 116/78; right leg 170 mm. systolic; left leg 145 mm. systolic.

Admitted into Royal Waterloo Hospital where the blood-urea was found to be 27 mgm. per 100 c.c., blood-calcium 10·6 mgm. per 100 c.c.

Blood-count.—R.B.C. 5,060,000; Hb. 100%; C.I. 0·97; W.B.C. 8,800. *Differential*: Polys. 60%; eosins. 3%; basos. 1%; large hyalins 8%; lymphos. 28%. Red cells normal; platelets normal.

Patient has used bandages for some time, but she says that they are of limited use. At present she is taking pituitary whole gland ½ gr. twice daily.

Dr. J. D. ROLLESTON said that in 1917 he had shown a case of Milroy's disease before the Section.[1] In his opinion no treatment was really required, as the disability in these cases was so slight, and in view of the fact mentioned by Milroy in a recent paper[2] that no autopsy had ever been performed on a case of his disease, no scientific treatment could be carried out. As Milroy had shown, a life of activity and distinction was quite compatible with this condition.

Coarctation of the Aorta.—TERENCE EAST, D.M.

Male, aged 55. First noted attacks of fluttering in the chest some weeks ago. These have not been observed, but appear to have been due to paroxysms of auricular fibrillation. Gets tired easily but capacity for exertion not much limited.

Served twelve years in the Navy; always healthy. Last of six children.

There are some large veins over the upper part of the sternum. In the left supraspinous fossa there are large arteries palpable, with a systolic thrill and a systolic murmur. Around the left clavicle there are the same signs, but less easily perceived.

The pulses are unequal and the right is later than the left. Blood-pressure, left arm 195/145, right arm 135/100. The femoral blood pressure is 140/105. The heart is enlarged, with extensive apex beat, which is rather weak, the first sound being reduplicated to form a gallop rhythm, and the aortic second loud. Rate 80, rhythm regular.

Skiagram shows enlargement of the left ventricle; the posterior part of the arch of the aorta hardly appears. The under borders of the upper ribs on the left side show the characteristic notching caused by the presence of large intercostal arteries acting as a collateral circulation to the descending aorta (fig. 1). Ascending aorta not enlarged.

Electrocardiogram is of the left ventricular type with abnormality in the T waves in the first and third leads, associated probably with the changes in the left ventricle following the high blood-pressure (fig. 2).

Wassermann reaction: negative. Urine: normal.

The signs are typical of coarctation of the aorta. The raised blood-pressure in the upper circulation is found in some cases, and failure of the left ventricle or cerebral hæmorrhage may occur.

1 *Proceedings*, 1916-17, x (Clin. Sect.), 39.
2 *Journ. Amer. Med. Assoc.*, 1928, xci, 1172.

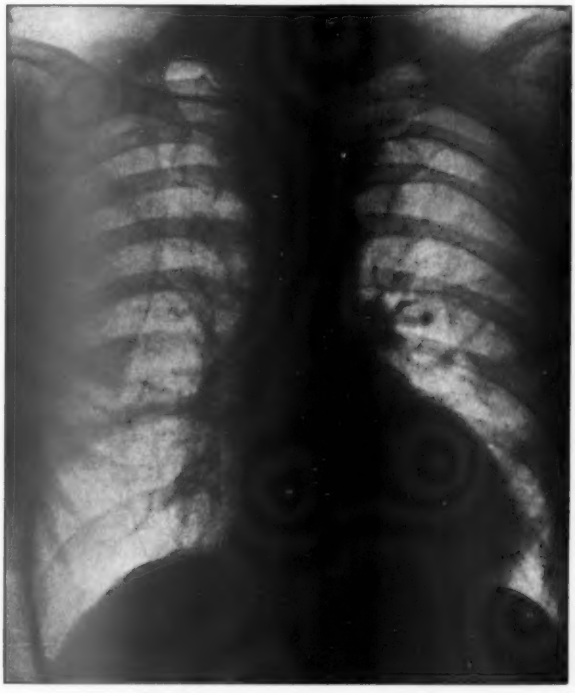


FIG. 1.—ANTERO-POSTERIOR VIEW.
Note absence of aortic prominence and the notching of lower edges of ribs.

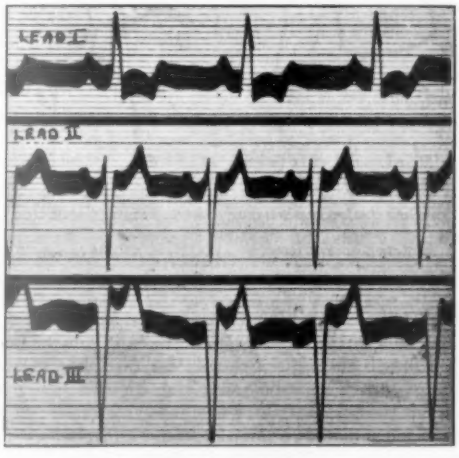


FIG. 2 (retouched).
Note preponderance of left ventricle and abnormal T waves.

The great difference in the blood-pressure in the two arms is curious. It may possibly be explained by reference to the case from which a specimen is about to be described.

Coarctation of the adult type, where there is a constriction as a rule just below the point of entry of the ductus arteriosus, is by no means incompatible with long and active life.

Specimen of Coarctation of Aorta.—TERENCE EAST, D.M.

Female, aged 46. Died from fracture of skull soon after admission to hospital. Clinical history unknown.

Specimen shows coarctation of aorta just below point of entry of closed ductus arteriosus: calcification at this spot. The ascending aorta is not enlarged. The aortic valves are normal, there is possibly slight hypertrophy of the left ventricle. There is slight aortic atheroma. The right common carotid arises directly from the aorta and bifurcates in the usual way. The left common carotid arises near it.

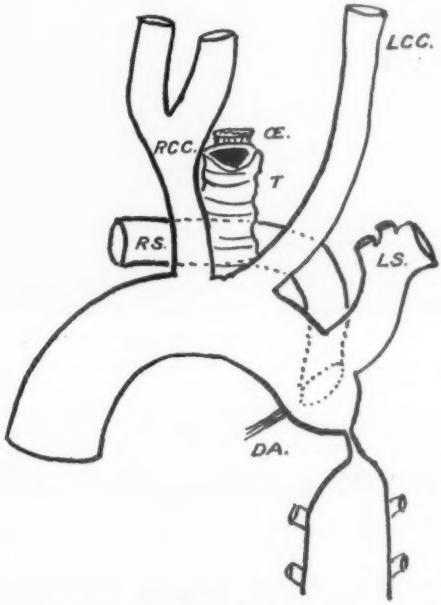


FIG. 3.—Coarctation of aorta and aberrant right subclavian artery.
D.A. = Ductus arteriosus. R.S. = Right subclavian. L.S. = Left subclavian.
L.C.C. = Left common carotid. R.C.C. = Right common carotid.

Then arises a large left subclavian artery, with very large branches. Then from the back of the aorta, just above the coarctation there is a large vessel, nearly as large as the aorta which runs to the right behind the œsophagus and supplies the right arm, taking the place of the right subclavian (fig. 3).

The branches of the thyroid axis and the internal mammary arteries were very large on both sides, as were also the long thoracic and posterior scapular.

Associated abnormalities: Infantilism, minute ovaries and infantile bicornute uterus; osteitis deformans of right tibia and skull.

The obliteration of the aorta just below the junction of the ductus arteriosus is characteristic of the adult type of the deformity. Although extensive abnormalities of the rest of the arch and great vessels are commonest in the infantile type, yet they are not very rare in the other.

In this case the anomalous vessel is similar to that reported by Fawcett[1]. It has been suggested by Maude Abbott[2] that in this instance the proximal part of the fourth primitive arch on the right side is missing, for it should form the subclavian artery.

With such an anomaly it is possible that the weak right pulse in the case described above may be explained. Where the pulses are uneven the left is usually the weaker.

The presence of such anomalous vessels as the one described suggests that the coarctation of the aorta is not a mere extension of the post-natal obliteration of the ductus arteriosus into the aorta, but some more primitive fault in development, at any rate in some instances.

Dr. WILLIAM EVANS: It is important to recognize, in the first place, that a slight and gradual diminution of the calibre of the vessel at the aortic isthmus is a common finding in the newly-born, when examined at necropsy. This narrowing, which is associated with a patency of the ductus arteriosus, is corrected early in life and the arterial lumen widens as the obliteration of the ductus proceeds. This condition is to be regarded as a physiological one, and must not be included in the group to which Dr. East's two cases belong, in which the congenital anomaly exists in an accentuated and persistent form.

Bonnett's classification of these cases into "adult" and "infantile" type is not helpful in the diagnosis and differentiation of this condition during life. The terminology is also

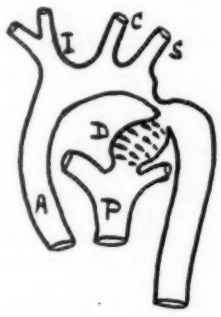


FIG. 1.—To illustrate the arrangement of the greater vessels in cases of congenital stenosis of the aortic arch classified as Type I.
A. = Ascending aorta. P. = Pulmonary artery. I. = Innominate artery.
C. = Left common carotid artery. S. = Left subclavian artery. D. = Ductus arteriosus.

misleading, in that the "adult" type occurs in infants under two years old, while the "infantile" is not infrequently found in adults. It is possible to define three varieties according to the anatomical deformity present, and the recognition of these groups may help in the diagnosis of this condition during life.

I have recently studied seven cases which belong to Type I. In this group congenital stenosis of the aortic arch is associated with patency of the ductus arteriosus, and it differs from the physiological type in three important respects in that the constriction is more abrupt, is persistent and is usually associated with hypoplasia of the proximal portion of the aorta and correspondingly of the left ventricle. There is relative hypertrophy of the right ventricle (fig. 1). During life these are recognized as cases presenting patency of the ductus arteriosus, but the congenital aortic stenosis is usually only discovered at necropsy, as in such cases a collateral circulation does not become established.

[1] Fawcett, J., *Guy's Hosp. Rep.* 1905, lix, 17.
[2] Abbott, M., *Amer. Heart Journ.*, 1928, iii, 404.

I have also studied nine cases which belong to Type II, and Dr. East's two cases would fall into this group. In these, congenital stenosis of the aortic arch (and occasionally actual atresia) is associated with a closed ductus arteriosus. There is hypertrophy of the proximal portion of the aorta and the left ventricle (fig. 2). A collateral circulation becomes established. The brachial blood-pressure exceeds the femoral. The radial pulse wave often precedes the femoral. Radioscopy may show absence of the aortic knuckle to the left, prominence of the ascending aorta to the right, hypertrophy of the left ventricle and erosion of the lower border of the ribs by hypertrophied intercostal arteries.

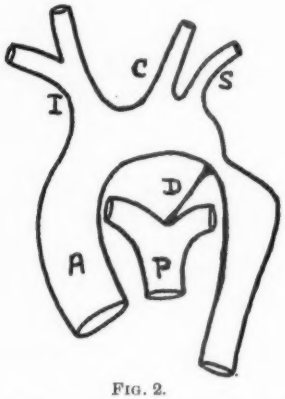


FIG. 2.

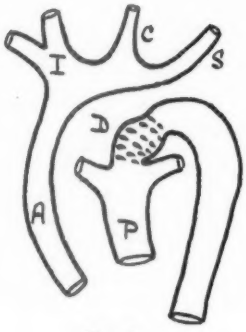


FIG. 3.

FIG. 2.—To illustrate the arrangement of the greater vessels in cases of congenital aortic stenosis classified as Type II.

FIG. 3.—To illustrate the arrangement of the greater vessels in cases of congenital aortic stenosis classified as Type III.

The abnormal artery in Dr. East's second case is the right subclavian which not infrequently assumes this origin and crosses behind the œsophagus to the right side.

In cases grouped as Type III, there is complete interruption of the aortic arch. It is a rare anomaly, but I have met with three cases. In such cases the pseudo-arterial arch is formed by the pulmonary artery and a widely patent ductus arteriosus which is continued into the descending thoracic aorta (fig. 3). The true aortic arch only carries blood for its brachio-cephalic branches.

An old Case of Pernicious Anæmia.—F. PARKES WEBER, M.D.

Mrs. L. W. (formerly L. P.), now aged 63½. I showed this patient under the heading "Enlargement of the Spleen and Liver with Pernicious Anæmia," in April, 1908, at the Medical Society of London (*Transactions*, 1908, xxxi, p. 389). The blood-count (January, 1908) had given: hæmoglobin 18%; erythrocytes 900,000; colour-index 1·0; leucocytes 6,000 (eosinophils 0·8%; basophils 0·4%; polymorphs 46·0%; lymphocytes 45·6%; monocytes 7·2%); 8 megaloblasts and 16 normoblasts were seen during the count of 500 leucocytes; much poikilocytosis; anisocytosis; polychromasia; basophilia punctata; no myelocytes. "Fragility" of erythrocytes was very slightly, if at all, in excess of the normal. There was a sub-icteric tinge. The spleen reached almost to the anterior superior iliac spine, and the liver was somewhat enlarged. An ordinary test-breakfast showed absence of free hydrochloric acid. The treatment was by atoxyl, and an acid pepsin mixture with meals. The great improvement that ultimately took place was chiefly after the atoxyl treatment had been discontinued.

Afterwards I felt uncertain in regard to the diagnosis, but fifteen years later, in 1923, when the patient was suffering from an anæmic relapse, I showed her at the

Section of Medicine, at the Royal Society of Medicine (*Proceedings*, 1923, xvi, p. 73), and in the discussion Dr. William Hunter carefully reviewed the whole data and present condition and summed up decidedly in favour of the case being one of pernicious anæmia. There was achylia gastrica (ordinary test-breakfast). A liver diet was afterwards found to be of great use, but during the last part of 1930 and first half of 1931, she took less liver and there was slight anæmia again. On November 7, 1931, she had again been neglecting the liver, and looked pale (sallow) and complained of feelings of faintness, palpitation on exertion, and "pins and needles" in the fingers. Blood-count: hæmoglobin 62%; erythrocytes 2,800,000; colour-index 1·1; leucocytes 4,950; slight anisocytosis and poikilocytosis. No enlargement of her spleen or liver detected. On December 5, after taking more liver (½ lb. every day except Sundays) in her diet, the erythrocyte count was 4,280,000; the leucocytes were 5,300, of which 9% were eosinophils, doubtless owing to the liver diet.

On January 30, 1932, after continuing the liver diet, the patient felt quite well. The erythrocyte count was 4,900,000 (hæmoglobin only 76%), and the leucocytes were 6,500. The red cells appeared normal, and included 1% reticulocytes; no erythroblasts. The thrombocyte count was 320,000. The "fragility" of the erythrocytes was within normal limits, hæmolysis commencing with the 0·5% sodium chloride solution (complete with the 0·38% solution). The Hijmans van den Bergh reaction was negative direct and strongly positive indirect, as it has always been. The urine showed only slight excess of urobilinogen.

Fractional examination of the patient's gastric contents was carried out on May 16, 1931, and on February 13, 1932, and on both occasions (even after a subcutaneous injection of histamine) there was complete absence of free hydrochloric acid. On the latter occasion pepsin was likewise tested for and found to be absent, at least by careful observation, up to twenty-four hours.

Orthostatic Œdema of the Dorsum of both Feet of the Nonne and Milroy type.—F. PARKES WEBER, M.D.

The patient, a young woman, (E.W.), aged 28, unmarried, is normally developed, except for moderate spinal scoliosis, and has enjoyed good health. The œdema of the feet, of which she now complains, gradually developed at about the age of 22. It is chiefly marked on the dorsum and always entirely disappears after rest in bed. There is no affection of the thoracic or abdominal viscera; no enlargement of lymphatic glands; no orthostatic albuminuria. The blood-Wassermann reaction is negative. There is no family history of any similar œdema. She has no brothers; her only sister, aged 16, has at all events not as yet developed anything of the kind.

The case seems to me to be one of œdema of the Nonne and Milroy type, though no other members of the patient's family are affected. (Cf. F. P. Weber, "A Note on the Nature of the Milroy-Nonne Disease," *Brit. Journ. Child. Dis.*, 1929, xxvi, p. 204.) The distribution in the feet rather than above the ankles is unusual; the type of shoes worn has doubtless something to do with this.

Intrathoracic Growth of Uncertain Nature.—HUGH S. STANNUS, M.D.

Male, aged 51, a waiter.

Wife and only daughter died of phthisis. Patient suffered from an attack of pneumonia with pleurisy in 1921. He denies syphilis.

His present illness began six months ago with cough accompanied by thoracic pain and sweats coming on in attacks at intervals of three and four days. At the beginning an attack lasted an hour, more recently for 24 to 36 hours. The pain is generally in the region of the left nipple or between this point and the sternum, deep but does not radiate, is sometimes of a stabbing character, causing considerable distress and cough but not expectoration. Between attacks he feels well; his

appetite is good; there has been no loss of weight (9 st.). Cardiac signs appear normal—no murmurs, thrills or abnormal pulsation or distension of veins noted. Pulse at wrists normal in all respects; 80 to 60 per minute. Blood-pressure: 70/100; radial arteries not thickened.

Physical signs in reference to the lungs are normal except over an area on the left side between the third and fifth ribs in front where breath-sounds, voice-sound and vocal fremitus are diminished and there is impaired resonance to percussion. On a single occasion (23.1.32) some drops of bright blood were coughed up. Sputum negative for tubercle bacilli. Tracheal tugging not elicited.

Nervous system:—Pupils equal and regular but small; right reacts to light readily, left less readily; neither reacts to accommodation. The cilio-spinal reflex, knee-jerks and ankle-jerks are absent. The plantar reflex is flexor on both sides, the abdominal reflexes and biceps-jerks are present, no Rombergism. Abdominal viscera normal. Bowels regular. Urine normal. Blood-count: R.B.C. 4,040,000; Hb. 98%; W.B.C. 12,000; differential count normal. Meinicke reaction negative.

Patient entered hospital, December 19, 1931. Just before and just after the New Year attacks were more frequent. On January 5, 1932 treatment with potassium iodide was begun, 20 gr. thrice daily increased to five times daily, since when the attacks of pain have been less frequent and less severe.

Skiagram shows a shadow with clear-cut outer rounded border continuous with that of the great vessels and the heart.

Discussion.—Dr. L. S. T. BURRELL said that the case might be one of non-malignant tumour. The sharpness of the skiagram suggested this rather than glands or malignant growth. He thought it would be useful to collapse the lung by pneumothorax and then to make another X-ray examination in order to see whether the mass was extra- or intra-pulmonary. With the lung collapsed it would also be possible to make an examination through the thoracoscope.

Dr. J. D. ROLLESTON said that he was interested to see that the patient was a waiter, in view of the fact that among the causes alleged for the recent increases in the frequency of primary carcinoma of the lung was the greater consumption of tobacco and particularly inhalation of cigarette smoke, whether by the smokers themselves or by those who by reason of their occupation had to live in a smoke-laden atmosphere.[1]

Hæmolymphangeioma of Tongue.—HAROLD EDWARDS, M.S.

Woman, aged 29. When two years old had partial glossectomy for hæmolymph-angeioma of the tongue. The whole tongue and the floor of the mouth are now covered with growth, which is at present stationary, and has remained unchanged for several years.

Result of Whitehead's operation for Carcinoma of the Tongue Nineteen Years Ago.—HAROLD EDWARDS, M.S.

Man, aged 78. In 1913 the right half of the tongue was removed on account of carcinoma, and fourteen days later the glands on the right side of the neck were removed. The pathological report on the tongue growth was squamous-celled carcinoma. No microscopic evidence of secondaries in the lymphatic glands removed was found. Four months after the second operation a recurrent mass was removed from the neck.

The function of the remaining portion of the tongue is now excellent, and there are no signs of recurrence.

Severe Prolapse of Rectum, which has resisted all forms of operative treatment.—HAROLD EDWARDS, M.S.

Man, aged 26. When 17, suffered from prolapse of rectum when working on a sheep farm in Australia. Has had eight operations for this, including abdominal rectopexy in March 1931.

1 Hoffman, *Ann. Surgery*, 1931, xciii, 56.

The sphincter is patulous, and the peri-anal skin thickened. On straining, about six inches of the rectum prolapse. The prolapse can be reduced without difficulty by the patient. Defæcation always produces prolapse, which is extremely painful.

Striæ Atrophicæ following Rheumatic Fever.—J. D. ROLLESTON, M.D.

The patient, a man aged 21, was admitted to hospital on September 26, 1931, certified to be suffering from diphtheria, but was found after admission to have rheumatic fever which became complicated by endocarditis, albuminuria and pleuro-pneumonia. The temperature pursued an irregular course, oscillating between normal and 104·6° F., until November 17, the fifty-eighth day of disease, when it finally became normal. The striæ which were situated on the back, arms, buttocks

Striæ atrophicæ following rheumatic fever.

and thighs were first seen on October 30, the thirty-seventh day of disease. On the back they extended from the level of the lower angle of the scapula to that of the lumbar vertebræ, were transverse in direction, pinkish or livid red in colour, depressed below the level of the normal skin and measured from 1 to 2½ in. long and about ¼ in. broad. On the left side they extended lower down than on the right and passed round to the ventral aspect. On the buttocks and posterior part of the thighs their arrangement was longitudinal.

A few faint striæ were seen on the posterior aspects of both upper arms.

Dr. F. PARKES WEBER said he thought that the complicating pleuro-pneumonia had more to do with the production of the striæ atrophicæ than the rheumatism had. He had never seen or heard of cutaneous "striæ" following uncomplicated rheumatic fever. Doubtless the age of the patient (for he was still in youthful bodily development) likewise favoured the development of the "striæ."

Unequal Radial Pulses with Intermittent Claudication of Right Leg.—H. AVERY, M.R.C.P.

H. G., a Hebrew, aged 62, tailor. Has been complaining for some years of cough and expectoration, but has had no hæmoptysis. For three months he has had pain in the right calf on walking, so that he requires to rest for about a quarter of an hour after each five minutes of walking.

There is also pain in the chest and shoulders, with marked hyperæsthesia, especially on the left.

There is no past history or family history of importance.

Examination revealed a marked inequality of the pulses, the right being synchronous with, but much weaker than, the left. The pupils were normal, no leucoplakia present. The heart slightly enlarged, the brachial blood-pressure was 125 mm. Hg systolic, 75 mm. diastolic on the right, and 175 mm. systolic and 75 mm. diastolic on the left. There were marked signs of chronic bronchitis. The dorsalis pedis artery was not palpable in either foot.

Skiagrams revealed no abnormality of the aorta or great vessels, no neoplasm of lung and no cervical rib. Bronchial tree striation is marked. Marked spondylitis.

The Wassermann reaction was negative. Sputum contains no tubercle bacilli.

This is probably a case of asymmetrical atheroma.

Dr. PARKES WEBER said he thought that, owing to the patient's age, arterial atheroma was the most probable cause both of the unequal pulses and of the intermittent claudication in one leg. Atheroma at the origin of the innominate artery might have caused local stenosis, so as to make the right radial pulse smaller than the left.

Suprarenal Virilism (Pubertas Præcox).—H. S. LE MARQUAND, M.D.

Patient, a male child, aged 2 years and six months.

History.—Parents are normal and come of healthy yeoman stock. The child is the first and only one. Labour was uneventful and the baby weighed 7½ lb. The mother has had no miscarriages.

At about the age of three months the patient started vomiting and this proved rather intractable. When nearly twelve months old he was admitted to Guy's Hospital for a few weeks for this symptom. After discharge the vomiting ceased.

Pubic hair was first noticed at about the age of fourteen months; since then the development of the sexual organs and general bodily growth have proceeded at an abnormally rapid rate.

During the last few months his sexual proclivities have caused trouble. His parents state that he cannot be left alone with an adult woman because of the obvious sexual advances which he makes; he is not attracted by small girls. These statements have been corroborated by observation in hospital.

On examination (26.1.32).—A strong, active red-headed boy who appears to be between six and seven years old. Height, 3 ft. 5½ in., weight, 49 lb. (Average 2 ft. 11½ in., and 30½ lb.). Muscular development very pronounced, approaching the infant Hercules type. Mental development about that of a child of two; he is exceedingly mischievous.

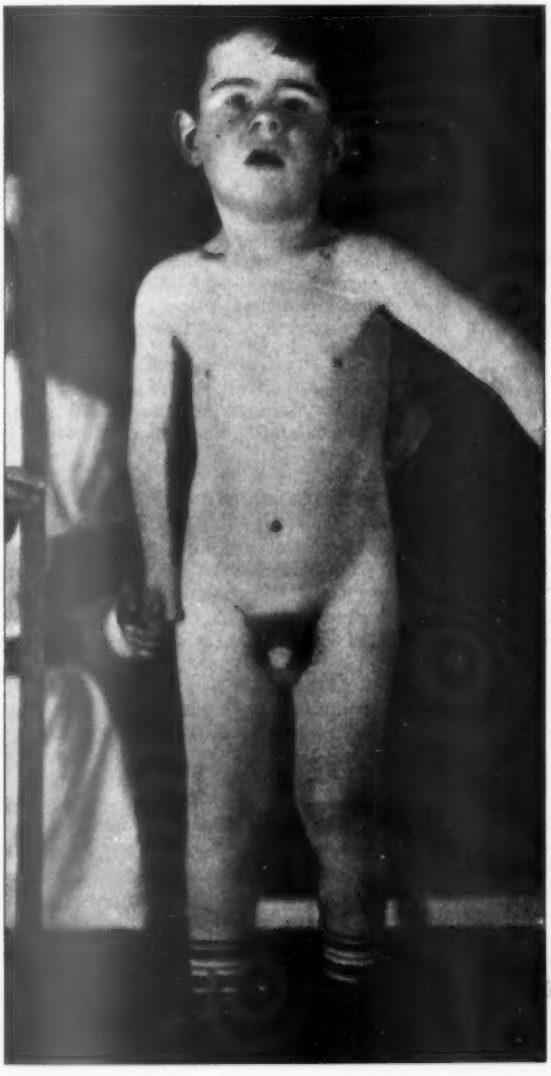
Development of hair.—Pubic hair well-marked with a horizontal upper limit. Hair prominent on forearms and legs below the knee, with a lesser distribution on the back and the thighs. No hair in the axillæ.

Genital organs.—The penis and scrotum are well-developed, almost the size of an adult, testicles descended and about half adult size.

Teeth show a complete first dentition.

No tumour can be felt in the abdomen but the patient resents examination in the region of the right kidney more than in that of the left.

The patient appears to correspond exactly with the cases described of virilism in children associated with tumour of the suprarenal capsules. In boys this is exceedingly rare. There are two instances of the removal of these tumours with recovery of the patients and regression of symptoms in baby girls (Collett [1] and Fordyce and Evans [2]).



Dr. Le Marquand's case of suprarenal virilism. The ink mark indicates 39 inches from the ground.

I have not found any reference to successful operation in the case of a boy. Collett [1] quotes five instances of operation on children which resulted fatally, death in most cases taking place suddenly a few hours after operation.

Skiagrams.—Abdomen : Nothing abnormal. Bones : All the carpal bones are more developed than normal for a child of 2½ years. This development corresponds to about the age of six years. The epiphyses of the elbow-joint also resemble those in a child of six years. There is a broad, wide line of condensed bone at the metaphysis of the radius and ulna. This appearance is similar to that seen in healed rickets. Skull : Pituitary fossa normal.

Urine.—Normal. *Blood-serum* : Sigma negative. *Blood-count* : R.B.C. 5,400,000 ; Hb. 100% ; W.B.C. 8,800. Differential : Polys. 39% ; lymphos. 51% ; eosinos. 1% ; monos. 9%. Blood-pressure : Systolic, 90 mm. Hg ; diastolic, 60 mm. Hg.

References.—[1] COLLETT, *Amer. Journ. of Dis. of Child.*, 1924-27, 197. [2] FORDYCE and EVANS, *Quart. Journ. of Med.*, 1928, xxii, 557.

Dr. PARKES WEBER said that the boy clinically was of what he had called the "infant Hercules" type, supposed to be due to an "endocrine tumour" of the suprarenal cortex. The "infantile Hercules" type apparently occurred only in males, but the "precocious (plethoric) obesity" type occurred in male as well as female children.

In regard to the question of operation, it should be remembered that excision of an endocrine neoplasm of the kind probably removed at least four-fifths of the total number of cells secreting the particular hormone in question, and that might account for some of the cases of fatal collapse following operation. Perhaps the required hormone might be obtained in some way or other and injected into the patient at intervals after the operation. By way of comparison, one might recall that injections of "parathormone" prevented tetany and death, when too much parathyroid gland substance had been excised. But in the present case, would the required hormone be contained in a suprarenal cortical extract, or would adrenalin be of any use ?

Cough completely relieved by shortening of elongated Uvula.—Sir JAMES DUNDAS-GRANT, K.B.E., M.D.

A middle-aged man complained of tickling cough, especially on lying down at night, of four months' duration. In December, 1931, I shortened the elongated uvula with scissors, followed by the galvano-cautery. The patient reported the following week that the cough had ceased at once.

The case is one of a series of eleven, and shows the value of the operation.

Abdominal Tumour : Case for Diagnosis.—H. L. C. WOOD, F.R.C.S.

A woman, aged 38, married, complained of abdominal swelling, increasing in size for fifteen months. She has had aching pain and has lost weight, but never vomited. Micturition normal.

Previous history.—Laparotomy fifteen months ago for ? rupture of right kidney. Kidney found surrounded by blood-clot, and removed. (The report states that a normal kidney, with no rupture, was removed.)

On examination a right paramedian scar is seen, beneath which a firm, rounded swelling can be felt, which is mobile on respiration. A second swelling of similar shape is palpable to the left of the mid-line. Spleen is palpable, left kidney palpable. Wassermann reaction negative. Barium meal and enema negative. Skiagram of chest negative.

Blood-count.—R.B.C. 4,250,000 ; Hb. 64% ; C.I. 0·79 ; W.B.C. 6,000. *Differential :* Polys. 68·4% ; eosinos. 2·8% ; lymphos. 28% ; hyals. 0·8%.

Section of Comparative Medicine.

President—Dr. J. A. ARKWRIGHT.

[*January* 27, 1932.]

DISCUSSION ON *B. WELCHII* INFECTIONS IN ANIMALS AND MAN.

Mr. T. Dalling: The rôle played by *B. welchii* in the causation of actual diseases in domesticated animals has always been—and still is—open to a certain amount of doubt. The introduction of a culture of *B. welchii* under the skin of an animal produces gas gangrene of a readily recognizable type, and during the European War we saw much evidence of such infections. We have had experiences of the contamination with *B. welchii* of antigens, etc., prepared for horses and dogs, the injection of which produced the typical gas gangrene syndrome, sometimes ending fatally.

In cattle, blackleg, the main cause of which is *B. chauvæi*, and in sheep, braxy, with which is associated *vibrion septique*, have been investigated by many workers and some record the isolating of *B. welchii* from the various lesions. Weinberg and Ginsbourg (1926) published a table showing the findings of fourteen workers who investigated the bacterial flora of muscle samples from blackleg cases. Four found a small percentage of infections with *B. welchii*. In all, from only six of the 587 cases examined was *B. welchii* isolated. Miss M. Robertson, writing in the recent edition of the Medical Research Council "System of Bacteriology" says, "*B. welchii* has been found not infrequently accompanying both infection with *B. chauvæi* and with *B. œdematis maligni* (Zeissler, 1920 and 1923; Zeissler and Rassfeld, 1923). "Karmen and Siefried (1924) are of the opinion that *B. welchii* can attack both cattle and sheep as an independent infection causing a fatal gas œdema of the muscles in these animals and, in addition, a braxy-like condition of the fourth stomach of sheep." McEwen (1930) says: "Considerable attention has been given to diseases of cattle due to the anaerobic sporulating bacteria, but it is doubtful if *B. welchii* by itself produces disease in these animals. *B. welchii* has on occasion been isolated, along with other pathogenic anaerobic bacteria, from material derived from cases of blackquarter, Warringholz and Rassfeld (1924), Zwick (1924), Scott (1928), Weinberg and Nicheilesco (1928). A primary infection of cattle with *B. welchii*, if it does occur, appears to be of but little importance . . . *B. welchii* has been accused of being responsible for disease in sheep in comparatively few instances, and the frequency of these infections and the extent to which they occur must remain an open question until the results of carefully conducted investigations become available."

It would thus appear that true *B. welchii* plays little or no part in the causation of diseases of cattle or sheep of the blackleg type, or of the braxy-like disease of sheep.

Much has been written on the presence of *B. welchii* in the alimentary canal of animals and on its pathogenic influence in an already diseased intestine. *B. welchii*

may be present normally in the intestine of any animal, but true *B. welchii* infection from the alimentary canal does not seem to occur unless the intestine is already diseased. Niemann (1930) records the isolating of *B. welchii* from the various tissues of birds heavily infected with intestinal parasites. He states, "It would appear that *B. welchii* infection in the domesticated fowl is not a specific disease entity but a sporadic infection that may occur in a heavily parasitized flock." There is also a reference by Nakamura (1922) to a similar occurrence.

It seems reasonable to believe that if *B. welchii* be present in a diseased intestine in which conditions are suitable for the elaboration of its toxin, a true *B. welchii* toxæmia may result.

There are three diseases in sheep caused by organisms which, though bearing a strong resemblance to *B. welchii*, show some differences, and it is to these that we wish to refer chiefly. In this country a disease among lambs popularly termed lamb dysentery has occupied our attention for a number of years; it is caused by an anaerobe which has been tentatively named the "lamb dysentery bacillus" (*L.D. bacillus*). We have spent much time in studying lamb dysentery and the anaerobe associated with it. McEwen kindly gave us a culture of his *B. paludis* (C.T. 40) and Bennett sent us a strain of his anaerobe (R. 2.). We have compared these three cultures and shall refer to them in the course of this discussion.

The three diseases.—Gaiger (1920) first drew attention to the occurrence of lamb dysentery in Scotland, but it was not until 1926 that *we* were able to state definitely that we had reproduced lamb dysentery by the feeding of cultures of the *L.D. bacillus* to young healthy lambs. The disease appeared to be confined to the border countries of Scotland and England for some years, but recently it has extended to practically every county in this country. It is characterized by an enteritis varying from a mild congestion of the intestinal mucous membrane to a condition in which large tracts of the small and large intestine become necrosed and ulcerated. On the surface of the inflamed mucous membrane and in the ulcers, practically pure cultures of the *L.D. bacillus* are found. Of the many cases examined, in only about 8 per cent. have we found the organism invading the body tissues, e.g., liver, kidney, blood, &c., from which it could be isolated in pure culture. Young lambs only are affected. For some time it was thought that *B. coli* was in some measure responsible for the causation of the whole condition. Following this idea and after the *L.D. bacillus*, which was at that time thought to be a true *B. welchii*, had been found in association with the lesions, the theory was advanced that *B. coli* caused a primary inflammation of the intestinal mucous membrane and that *B. welchii*, which was also present, produced a fatal toxæmia. In 1926, however, we were able to show definitely that *B. coli* played no part in the causation of the disease and that the so-called *B. welchii*, which we now know to have some characteristic differences, was the sole responsible agent. The disease is now completely controlled, as methods have been devised for the treatment of lambs soon after birth with anti-serum from the *L.D. bacillus* and for the ewes with antigens which are injected prior to the birth of the lamb. Incidentally, we have shown that lambs born from highly immune mothers are still susceptible and that they only become resistant about four hours after they have partaken of the colostrum from such immune mothers.

In a private communication from Bennett, Western Australia, the disease with which his strain of *B. welchii*-like organism is concerned, is described simply as a "braxy-like disease." We infer from this that the disease is characterized by sudden death and a gastritis or enteritis.

A Comparison of the L.D. Bacillus, B. paludis *and Bennett's Anaerobe with* B. welchii.

Symmonds (1915) was the first to give a reliable description of the morphological characters of *B. welchii* and from a study of the "sugar" reaction he divided the various strains he studied into four groups as under:—

		Glycerine		Inulin
1	...	+	...	+
2	...	+	...	−
3	...	−	...	+
4	...	−	...	−

Since 1915 many workers have described *B. welchii* and the salient characters of the organism are well known. It is with the difference between the anaerobes under discussion and *B. welchii* that we are concerned.

In 1926 we summarized these differences in connection with the *L.D. bacillus* as under:—

	L.D. bacillus	*B welchii*
(*a*) Toxin	Highly potent	Potent
(*b*) Antitoxin	Neutralizes L.D. and *B. welchii*	Neutralizes *B. welchii* but not L.D.
(*c*) Solid serum	Liquefies	Does not liquefy
(*d*) Alkaline egg	Clots rapidly	Does not clot
(*e*) Glycerine	Does not ferment	Ferments
(*f*) Acrolein	Does not form	Forms

The toxin of *L.D. bacillus* is much more potent than any we have even been able to produce from any strain of *B. welchii* with which we have worked. Its preparation is simple. The toxin is also hæmolytic. High value antitoxin can readily be prepared in horses and can be shown to protect in small doses against many fatal doses of toxin and culture. A striking fact is that this antitoxin protects against ordinary *B. welchii* toxin or culture, but *B. welchii* antitoxin, even of very high value, does not protect against L.D. toxin. L.D. antitoxin also neutralizes the hæmolysin of both L.D. and *B. welchii*. *B. welchii* antitoxin similarly neutralizes its own hæmolysin and that of L.D. toxin, although it cannot neutralize L.D. toxin. This is the more curious since the hæmolysin in L.D. filtrate can be used as a measure of L.D. toxin.

L.D. bacillus is more proteolytic than *B. welchii*, as evidenced by its liquefying solid serum. With some strains liquefaction is slow, but appears after a sufficient period of incubation. Alkaline egg is clotted though some strains must be incubated for a prolonged period before positive results are found.

When grown on the usual range of "sugars," L.D. ferments those typically fermented by *B. welchii*. No strain of L.D. in our possession shows any indication of fermenting glycerine and because it also fails to ferment inulin, the organism falls into the Symmonds Group 4. In passing we may say that we have not been able to obtain from any laboratory anywhere examples of Symmonds Group 4. The acrolein test devised by Humphreys (1924) is negative for the *L.D. bacillus*.

The simplest explanation of the differences between this culture and *B. welchii* would be that the former consists of more than one anaerobe. In the study of our cultures every available technique, except the single cell isolation method, has been used to demonstrate this point and we have failed to show that the cultures are "impure." Furthermore, samples of the culture have been examined by several of the eminent anaerobe workers in this and other countries and, as far as we know, they have been unable to show the presence of more than one organism. From two Continental workers we have received strains of so-called "purified" *L.D. bacillus*; both strains, however, gave exactly the same results when examined by us as did the original cultures.

Bacillus paludis.—McEwen in his article on *B. paludis* refers to the *L.D. bacillus* and claims that the characters of the two bacilli, especially the active proteolytic properties of the *L.D. bacillus*, are sufficient to distinguish them. He also states that an antiserum made from *B. paludis* has no neutralizing effect upon cultures of *B. welchii*, and claims that this is a further distinguishing point between *B. paludis* and the *L.D. bacillus*. We have spent some considerable time in examining McEwen's culture, and have just published our results (1931). They clearly show that antigenically *B. paludis* and the *L.D. bacillus* are similar, i.e., L.D. antitoxin neutralizes the toxin of L.D., *B. paludis* and *B. welchii*; *B. paludis* antitoxin neutralizes the toxins of *B. paludis*, L.D. and *B. welchii*; *B. welchii* antitoxin neutralizes the toxin of *B. welchii*, but not the toxins of *B. paludis* or L.D. Experiments on the active immunization properties of *B. paludis* were also carried out, and we found that *B. paludis* and L.D. cross-immunize. Further, a small experiment carried out in sheep in a lamb-dysentery area a year ago, showed that ewes actively immunized with *B. paludis* formol culture gave protection to their lambs against lamb dysentery quite as effectively as did those immunized with L.D. anaculture. We agree with McEwen, however, that *B. paludis* ferments glycerine readily, but, in our hands, *B. paludis* has proteolytic characters similar to the *L.D. bacillus*, for if incubated for a sufficient length of time the culture will cause a liquefying of solid serum and a clotting of alkaline egg. We must conclude, therefore, that *B. paludis* differs from *L.D. bacillus* in one feature only, namely, that it ferments glycerine. It gives a positive acrolein reaction—this is to be expected, because the reaction is directly related to the growth on, and fermentation of, glycerine.

Bennett's anaerobe.—We have examined at length a culture (R.2), which we received from Bennett, in 1930. It shows typical *B. welchii* characteristics and ferments glycerine; it clots alkaline egg and shows some liquefaction of solid serum after prolonged incubation. It produces a toxin, but the toxin is much less potent than those of the "lamb dysentery bacillus," or *B. paludis*. The culture and its toxin, however, are neutralized by L.D. serum but not by *B. welchii* serum. A serum made in rabbits, using R.2 as an antigen, neutralizes L.D. and *B. welchii* toxins. R.2 toxin and antitoxin give complete cross neutralization with lamb dysentery and *B. welchii* cultures and toxins. Immunity experiments were carried out in guinea-pigs, and showed that there was some difficulty in immunizing these animals by the use of the R.2 antigen against L.D. or its own toxin. There was, however, some protection against both toxins. It would appear, therefore, that R.2 is a culture morphologically and culturally similar to *B. paludis*, except that the potency of its toxin is much less. This is, perhaps, an unimportant point, because strains of organisms vary considerably in toxicity. R. 2 shows the same differences from L.D. as did *B. paludis*, namely, it ferments glycerine, and is positive to the acrolein test.

It should be noted that in our study of these organisms no agglutination work has been done.

In sheep, therefore, we can recognize at least three diseases which are apparently caused by organisms bearing a striking resemblance to *B. welchii*. The differences between these organisms and typical *B. welchii* have puzzled us for some considerable time; we cannot offer any explanation of the antigenic differences. The "purity" of the cultures may be criticized; we cannot pretend to vouch for the purity of *B. paludis* or R.2, but we feel that in view of our lengthy study of this organism we are justified, until single cell isolation can be carried out, in concluding that our *L. D. bacillus* culture is pure. Another interesting feature is the distribution of these organisms. In any lamb-dysentery area the *L.D. bacillus* can be isolated from infected pastures. If the *L.D. bacillus* and *B. paludis* are closely related, it seems strange that the older sheep in a lamb-dysentery area do not fall victims to *B. paludis* infection. In these areas it is rare to find sheep over the "lamb" age

dying of any cause. Again, *B. paludis* must be present in many parts of the Romney Marsh and, as far as our information goes, there is not a heavy death-rate among lambs such as one finds in a lamb-dysentery area. An explanation of the former may be that the lambs become immunized on the lamb-dysentery infected land. This explanation, however, cannot hold good for the Romney Marsh.

Recently, another organism of the *B. welchii* type has been sent us from Victoria, Australia. It has been isolated from the intestine of young sheep which have suffered from a fatal enteritis. We have not yet had the opportunity of studying this organism fully.

We would conclude from our work that, though typical *B. welchii* may be isolated from sheep under normal and diseased conditions, it is probable that the *B. welchii*-like organism causing specific diseases in sheep varies somewhat from typical *B. welchii*. We venture the suggestion that the group of organisms referred to as *B. welchii* contains several antigenically and culturally different types.

Mr. A. D. McEwen: There is often no explanation why micro-organisms of the gas-gangrene group produce disease in animals. The causal organism of black disease of sheep may be found in the normal liver tissue of sheep in black disease areas. When these sheep are subjected to a liver-fluke infestation the immature flukes wandering in the liver injure the tissue and thus function as activators for bacterial spores lying latent in the liver. The spores germinate and further tissue destruction, toxæmia and death result. Here we have a remarkable explanation of why sheep succumb to infection with a bacterium of the *B. œdematiens* type.

On the other hand there is not even a plausible explanation to account for the invasion of the muscles with *B. chauvæi* in the disease blackquarter of cattle. Apparently the infection is not through any external wound. Possibly the bacteria gain access to the body via the alimentary canal, but what activates the bacteria which reach the voluntary muscles is not known. Like the other members of the gas-gangrene group, *B. chauvæi*, if washed, may be inoculated into the muscles without causing disease.

This same organism is the cause of gas gangrene of sheep, but here the infection is through wounds, and it is easy to understand the infection starting in injured tissue and spreading to surrounding parts.

The diseases bradsot, or braxy, and lamb dysentery are examples of alimentary infection with anaerobic bacteria, and with both diseases there are cases where there is invasion of the wall of the stomach or the intestine with the causal micro-organism before death. The former disease is attributed to *V. septique*, and the latter to a bacillus resembling *B. welchii*, but much more toxicogenic. These bacteria are no doubt frequently present as saprophytes in the intestine of animals. There has been no satisfactory explanation advanced to account for the bacteria acquiring the capacity to invade the wall of the alimentary tract.

The presence of the bacteria in the tissues and their production of toxin as they multiply in the tissues are accepted as sufficient explanation of the cause of the disease. As these bacteria do not invade healthy tissue unless in the presence of preformed toxin or some other activator, the question may be asked, what enables these bacteria to invade the tissues in the first instance? With braxy this difficulty has been admitted, and to meet it the suggestion has been made that ingested frozen food entering the rumen, climbs the adjacent walls of the abomasum, lowering their vitality, whereby the stomach wall becomes a prey to bacterial invasion. In view of the physiological arrangements of the ovine stomachs this explanation cannot be regarded as even probably the true one.

Hare and Glynn's studies on lamb dysentery are most interesting. They record a necrosis of the villi of the small intestine with petechial hæmorrhages and ecchymoses of that organ and in this primary lesion bacteria were not implicated.

When the intestine was ulcerated organisms resembling *B. welchii* were found in the walls of the ulcer and were regarded as secondary invaders. Mainly on histopathological grounds they compared the disease with melæna neonatorum noting similarities between the two diseases. It is interesting to note that a number of Continental workers have associated melæna with a heavy *B. welchii* infection of the intestine and Needleman on bacteriological grounds has drawn attention to the similarity of the disease to lamb dysentery as in both there may be a heavy intestinal infection with bacteria of the *B. welchii* type. From the researches of Dalling and his co-workers, it must be accepted that the lamb-dysentery bacillus is the causal organism. Nevertheless, Hare and Glynn are probably correct in concluding that the initial lesions are independent of any bacterial invasion of the tissues and the cause of these lesions has not been explained.

Let us consider the disease of sheep on the Romney Marsh popularly called "struck." This disease in many ways resembles lamb dysentery and it is suggested that "struck" is actually caused by the absorption of the toxin of *B. paludis* (a bacillus very similar to the *L.D. bacillus*) the toxin being produced by the bacillus growing in a pabulum of the contents of the intestine. Should this be correct, may not a similar process be at play in lamb dysentery? The disease "struck" is characterized by acute enteritis and peritonitis. Frequently the intestine is ulcerated. At the time of death, *B. paludis* is sometimes found in small numbers invading organs in the abdominal cavity, but in other cases the body tissues are sterile; when there is ulceration the bacteria may be seen invading the tissue at the periphery of the ulcer, but when there is no ulceration no bacteria are demonstrable invading the bowel and the intestinal lesions, as in lamb dysentery, are not due to bacterial invasion. Therefore "struck" may occur when the body tissues are sterile and the necrosis, hæmorrhage and other lesions are attributed to the action and absorption of toxin from the alimentary canal.

B. paludis toxin has been demonstrated in the contents of the intestine of sheep at the time of death. The disease has been produced by feeding large quantities of *B. paludis* broth culture, but it has not been produced by feeding the filtrate of such cultures.

Centrifuged bacteria resuspended in broth and fed to sheep produced the disease. Similar bacteria resuspended in normal saline did not produce the disease when fed.

It is possible that bacteria in the intestine only produce a sufficiency of toxin to cause disease under exceptional conditions, chief among these conditions being the presence of suitable food material in the intestine for bacterial growth and toxin production, and it may be that an alimentary disturbance is also necessary to provide conditions where toxin as it is produced is not destroyed by the digestive processes.

The failure of toxin in filtrates of broth cultures to produce disease when fed is attributed to destruction or absorption of toxin in the rumen and reticulum and to a lesser extent in the abdomen. In "struck" and possibly in lamb dysentery as suggested by Hare and Glynn the bacteria are truly secondary invaders, being secondary to their own toxin.

These suggestions find support in the work of Williams on obstruction. He concluded that the death of the patient was often due to absorption of *B. welchii* toxin from the obstructed intestine, the bacteria finding a suitable pabulum for toxin production in the contents of the obstructed bowel.

With the exception of diseases of alimentary origin such as lamb dysentery and "struck" the domestic animals are very rarely subject to infection with bacteria of the *B. welchii* type.

In a large number of examinations made upon sheep which have died from wound gas-gangrene on ground where struck is enzootic, the gas-gangrene has never been found to be caused by *B. paludis* or by *B. welchii*. Nevertheless, the unwary might conclude that *B. paludis* gas-gangrene was common because the musculature

of the "struck" sheep a few hours after death presents a picture which macroscopically resembles gas-gangrene and smears from the muscles show a rich infection with *B. paludis*. This, however, is entirely a post-mortem change.

Statements to the effect that *B. welchii* causes gas-gangrene in domestic animals can only be accepted when corroborative evidence rules out post-mortem invasion, and when the bacteriological data are sufficient to justify the recognition of the bacterial species. There are but few recorded cases fulfilling these requirements.

Miss Muriel Robertson: The *B. welchii* organisms form a group of extremely wide distribution, and also of curiously wide variation in toxicity and infecting power. Morphologically the bacillus stage is so characteristic and constant that to the eye there is a firm ocular basis for the collection that runs under the name. Its pathogenicity is so slight in some of the forms in which it is presented to both man and animals, that no milk sample under ordinary open conditions is free from it, and in America one of the salts commonly used in some districts to make bread rise was found to do this by means of the *B. welchii* organism present which multiplied and formed the requisite gas. The pathogenicity can, on the other hand, be so terrible that a man may die in eight hours from a fulminating gas gangrene set up by this organism in a wound which in itself is neither extensive nor serious.

The diseases produced by *B. welchii* in man are primarily the gas gangrenes with all their variations and complications, the acute intestinal conditions, and puerperal sepsis. I propose to leave all these in more competent hands. It is interesting in connection with the scope of the paper of the opener of the discussion to point out the less well recognized places in which *B. welchii* may turn up. I draw these from various sources and I propose to mention only a few. A chronic infection in the nose characterized by œdema, in a case of Dr. Elizabeth Lepper's, yielded a culture which I tested in all ways and found to be a typical averagely pathogenic *B. welchii*. Dr. Lepper has found another in a case of chronic throat infection. She tells me that she has found only two or three cases in which an organism of this kind has been present out of many hundreds of infected tonsils examined.

Samples of catgut were sent to be examined at the Lister Institute, owing to unsatisfactory results at a London hospital. The catgut was an iodized product kept in spirit. *B. welchii* was isolated by Dr. Mary Barratt from the thinnest of three thicknesses. Only a very few cocci were found in the aerobic cultures.

Finally, another case of rather particular interest was sent and worked out by Dr. Barratt. *B. welchii* was isolated from a catheter specimen of urine from a pregnant woman suffering from persistent vomiting; it was present in another specimen from the same case a week later, and two or three weeks after that *B. sporogenes*, *B. multifermentans* and *B. welchii* were all found. At the sixth month the patient gave birth to a dead fœtus. Samples of urine after her recovery no longer showed the organism.

I now turn to some of the cultural and antigenic characters. The *B. welchii* group can be held together loosely on morphology and more loosely on cultural characters, but when we touch on antigenic properties division quite as much as cohesion has to be accommodated in the collection.

In cultural characters an important variation is failure to clot milk in an otherwise quite characteristic organism capable of producing the expected lesions and death in susceptible animals. This strain is amenable to *B. welchii* antitoxin. In my experience one of these came from a virulent and fatal war gangrene and Stoddard described another under the name of *B. egens*. I also remember seeing one among a collection from gall-bladder infections in man shown at a laboratory meeting by Dr. Whitby some years ago.

The proteolytic character described by Mr. Dalling in lamb dysentery leaves me unconvinced. I think that it is due to the almost universal microbic association of the *B. welchii* group with a member of the proteolytic sporogenes group. It will be called to mind that for twenty years, in the hands of bacteriologists no less capable than ourselves, *B. welchii* and Fraenkel's bacillus as it was known in Germany was considered to be a proteolytic organism. Moreover, I have found exactly the same type of proteolysis in the diagnosis room cultures and in typical original *B. welchii* cultures from all sources. I have handled Mr. Dalling's cultures and I do not consider that there are two pathogenic organisms present, I think he has exactly the same type of symbiotic mixture with a sporogenes form as any other *B. welchii*. I consider that all he postulates about its toxin is probably correct but the proteolysis is not a sound distinction between L.D. and ordinary *B. welchii*.

In regard to the distinction between L.D. and *B. paludis*, I consider both these organisms to be culturally *B. welchii* group types. I made a simple full culture inoculation test in guinea-pigs and found that L.D. concentrated anti-serum in the big dose of 5 c.c. delayed by twenty-four hours only the death from *B. paludis* while completely protecting against L.D. The experiment has not been repeated and is therefore open to criticism.

I have on several occasions carried out this type of experiment with L.D. and *B. welchii* and obtained results in exact agreement with Mr. Dalling, i.e., L.D. anti-serum will stop *B. welchii* but not the converse.

I should like in conclusion to add a few points purloined from my colleague, Dr. Felix. In the *B. welchii* group we have no H-antigen and therefore no large-flaking agglutination. The O-antigen from *B. welchii* from human sources differs in different strains to a much greater extent than in *B. tetani* or *V. septique*; in other words type specificity is highly developed. This low degree of community of the O-antigen is particularly well marked in agglutination tests with monovalent horse and rabbit sera, complement-fixation tests tend to reveal more overlapping than do the agglutination results.

If other anaerobes, for example, *V. septique* and *B. tetani* are used along with *B. welchii* in complement-fixation, overlapping of the O-antigen between the three species is frequently found so that neither agglutination nor complement-fixation affords a reliable method of differentiation between *B. welchii* and other anaerobes.

B. paludis and B.L.D. when included in tests along with *B. welchii* show a more close relation to each other than to the *B. welchii* of human origin. This is shown by their having a greater community of antigen with *V. septique*. Complete cross-agglutination tests have not so far been done.

The *B. welchii* group would sum up as a collection of organisms composed of at least two large subgroups: (1) *B. welchii* mostly of human origin, the members differing in serological type on their O-antigen among themselves but producing one *B. welchii* toxin. (2) A second subgroup L.D. derived from sheep marked also by variation in the O-antigen and while bound together within itself it is divided from the first subgroup by the more comprehensive though related character of its toxin. *B. paludis* either forms a third division or drops into the second.

Mr. B. W. Williams: In animals it appears that there are specific diseases which are attributable to *B. welchii*, or to varieties of *B. welchii*. In man, on the other hand, *B. welchii*, so far as I am aware, only takes part in human disease as a complication of some injury or other illness.

There is a further difference between human infection and experimental infections in animals. Experimental animals, such as the mouse, pigeon, and guinea-pig, are selected because of their extreme susceptibility to infection. Man appears to be relatively insusceptible and the presence of a small contamination of *B. welchii* will not cause a material infection, except under special circumstances.

B. welchii is, I believe, responsible for an important part of the toxæmia associated with acute intestinal obstruction and ileus. In these conditions the bacillus is proliferating in the stagnant contents of the intestine, and the absorption of the toxin gives rise to symptoms without material bacterial invasion of the tissues. To-day we are concerned with the infection of human tissues with *B. welchii*.

B. welchii contamination in man nearly always results from the infection of a wound, accidental or operative, with material containing the organism or its spores. The very wide distribution of the organism in dust, soil, milk, and fæces, means that this contamination may occur in a great variety of circumstances; it is, however, possible to group the cases roughly into classes which differ somewhat in their pathology and treatment.

The best-known group is that in which contamination occurs as a result of accident or injury. To this group belongs the war-wound type of gas-gangrene. The contamination most probably consists of spores, and infection will only result if there is a nidus in the form of foreign bodies, dead or damaged tissue, in which proliferation and toxin formation can begin. Complete early surgical excision of the dead and damaged tissue, in the absence of tension or any other factor which is likely to impair the circulation, will always avoid a serious *B. welchii* infection. Mild transient infections may occur.

The next group, which results from the contamination of wounds with intestinal contents, is much less generally recognized. In this group the contamination often contains *B. welchii* in the actively proliferating vegetative form, and when there is intestinal obstruction the toxin also may be present. On the other hand, there is usually very little dead or damaged tissue and the abdominal wall, the most common site of these infections, has an excellent and unimpaired blood-supply. It follows therefore that there are occasional cases in which severe gas-gangrene develops, but there are an enormous number of mild or transient infections which probably are not recognized. A mild or transient anaerobic infection, however, is usually succeeded by an aerobic pyogenic infection, which may be extremely severe, or even fatal. It is suggested that it is the damage done by the transient anaerobic infection which often determines the severity of the subsequent pyogenic stage.

A third well-defined group of cases is that which occurs as a puerperal infection, usually arising in cases in which there has been obstetrical interference after the death of the child. This group has been discussed in another section by Dr. Wrigley.

Lastly there are a certain number of cases in which *B. welchii* appears as a terminal infection in a patient dying from some other disease.

Diagnosis.—The diagnosis of *B. welchii* infections of the gas-gangrene type has been fully described in the literature of war wounds and elsewhere. This is, however, a late stage and, short of heroic operative removal of infected tissue, there is little scope for treatment, even with modern sera. Further, except in injuries of the limbs, as in the first group of cases, there is little scope for heroic surgery. It is therefore proposed to discuss the diagnosis of the earliest stages of anaerobic infection, as typified in the bowel-contamination group of cases.

After operations such as the removal of a gangrenous appendix, or for acute obstruction caused by carcinoma of the large intestine, or a strangulated umbilical hernia, it will frequently be found that in from twelve to twenty-four hours the area about the wound becomes infiltrated, with a sluggish cellulitic appearance and is tender, and that there is a serous exudate, often brownish, containing droplets of free fat and occasionally a few bubbles. After from twenty-four to forty-eight hours a coppery discoloration appears and, if the infection is in the deeper layers, may appear first at fascial attachments, such as the iliac crest or round the umbilicus. This discoloration is accompanied by a palpable thickening in the tissues and is in reality an anaerobic cellulitis, as can be shown by culture of a drop of fluid obtained by

puncture with a fine needle. At this stage, as a rule, the anaerobic infection subsides and pus cells appear in the exudate, as the pyogenic infection begins to take its place. Occasionally the anaerobic infection persists and spreads, and definite constitutional signs of anaerobic toxæmia begin to show.

Now, severe welchii infections are always accompanied by enormous local proliferation of the organism, and I believe that it is possible, by careful observation of the local condition and examination of the exudates, to anticipate by some all-important hours the development of a severe welchii infection. Unfortunately, the bacteriological identification of *B. welchii* is not a very simple matter, and skilled bacteriologists, particularly those skilled in anaerobic work, are not always available at short notice. In the time occupied in culture, or even animal inoculation, the patient either recovers or, sometimes, gets beyond the scope of treatment. Also, it is the relative abundance of *B. welchii* in the fresh exudate which is of importance. During the examination of a considerable number of such exudates stained by Gram's method, I have found that the presence of the spotted form of the bacillus could always be taken as evidence of the presence of *B. welchii*. This form is much more common in exudates than in cultures. Thus, with a little practice, it is possible in a very short time to make a reasonably certain diagnosis of the presence of *B. welchii*, and to form a fair estimate of the numbers present. In an ordinary smear-film, I should regard the presence of one bacillus resembling *B. welchii* under each field under a 1/12th objective as being indicative of a severe infection requiring immediate serum treatment and such measures to ensure free drainage as circumstances may allow.

The first step in making an early diagnosis of *B. welchii* infection is, of course, remembering the possibility of its occurrence.

Mr. Dickson Wright said that the organisms of the *Bacillus welchii* group were widely distributed in nature. They were normal inhabitants of the alimentary tract of man and most animals. The heavy infection with *Bacillus welchii* of the liver of the dog explained the phenomenon of "autolytic peritonitis." Gordon Taylor and Whitby had found the organism in the interior of gall-stones and in gangrenous cholecystitis. Evidence was now accumulating that in many animals the organism was almost a normal inhabitant of muscular and other tissues. The production of "autolytic peritonitis" in dogs was the starting point in these discoveries. This form of peritonitis was produced when a piece was removed from a dog's liver and dropped into the free peritoneal cavity; the animal invariably died within twenty-four hours from generalized peritonitis due to the *Bacillus welchii*. If another dog was injected intraperitoneally or intravenously with thousands of millions of the living organisms which had killed the first dog, it literally did not turn a hair! It was soon found that the same form of peritonitis was produced with autoclaved liver, sterile liver extracts, sterile bile. Andrews, Rewbridge and Hrdina had recently shown that if a dog's bile was diverted into the pleural cavity or the muscles, a local condition of fatal gas gangrene developed, although the bile itself was sterile. Even a sterile solution of bile salts gave the same results if sufficient quantity was employed. Moreover, these workers had found that the introduction of muscle, freshly-ground in a mortar, into the peritoneal cavity, produced a typical autolytic peritonitis, but if the muscle was autoclaved this did not take place. The crucial experiment was one in which six dogs had a leg constricted by a wire for twenty-four hours without breaking the skin. Into three of the legs a sterile liver extract was injected. After twenty-four hours the dogs were killed, and the control legs showed normal gangrene, the injected legs typical gas gangrene. These experiments confirmed in a striking fashion the discovery of anaerobic bacteria by Keith, in the muscles of hogs, guinea-pigs, rabbits, &c.

In man gas gangrene might develop in the most mysterious manner. He, the speaker, and others had seen it in a contused limb without any break in the skin; it occurred in a most annoying way after certain operations such as amputations, simple cholecystectomy, appendicectomy and even tonsillectomy. The possibilities of the method of infection in post-operative gangrene were that the organisms (1) got into the tissues from a neighbouring viscus such as appendix, gall-bladder or colon when the operation had involved the opening of that viscus; (2) got in from the skin, instruments or the catgut; (3) were dormant in the tissues and were activated by operative or other trauma. The organisms might have found their way as a result of a previous septic wound in another part of the body or from the alimentary canal. In this last respect Arnold had shown quite conclusively that when the chyme had a pH of 8 the lymph in the thoracic duct contained 500 to 1,000 organisms per cubic centimetre. Was it not possible that the body could deal with all the living organisms that entered in this way, except the spore-bearers which were so tenacious of life?

In any case the eccentric behaviour of the bacillus of Welch, under different circumstances, provided one of the greatest mysteries of bacteriology requiring elucidation at the present time.

Mr. Humphrey Neame stated that *B. welchii* infection of the human eyeball was a rare occurrence. Cases were occasionally reported in the ophthalmic literature—for example that by Heath [1] in which a labourer was injured while chipping concrete with hammer and chisel. He was seen within twenty-four hours. Within a few hours of his admission to Hospital, he looked ill; his temperature was 98·2° F. and his pulse 90. There was rapid development of chemosis and œdema of the upper lid and some proptosis. A bubble of gas could be seen occupying the greater part of the anterior chamber. Evisceration of the eyeball, coupled with intramuscular injection of 25 c.c. of anti-gas serum (welchii) and 10 c.c. into the orbit, was followed by subsidence of the inflammation and uneventful recovery. An organism with the characters of *B. welchii* was recovered from the vitreous.

Similar cases have been reported by James [2] and Ridley [3].

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Mrs. Ivens-Knowles said that cases of gas-gangrene of the pregnant uterus were often associated with a dead fœtus. She had reported such a case which had been successfully treated with Weinburg serum from the Pasteur Institute. The patient had been four days in labour under the care of a midwife, and forceps delivery had been attempted ineffectually. On admission to hospital the child was dead and there was a putrid vaginal discharge. After craniotomy, 20 c.c. of anti-gangrene serum, 20 c.c. of anti-coli serum, and 30 c.c. of anti-streptococcal serum were given. From the lochia *B. welchii* and *B. coli* were isolated by animal inoculation. The tissues of the cervix, vagina and perinæum were swollen and gangrenous, the patient was toxic with rapid pulse and low temperature but made a good recovery.

In Australia cases were relatively common following criminal abortion and were believed to be due to the introduction of fæcal specks on the instruments employed. She, Mrs. Ivens-Knowles, had treated a large number of cases of gas-gangrene during the European War, and agreed that the organisms often proliferated in the tissues with alarming rapidity. In a typical case the skin became lemon yellow, the pulse was rapid and the temperature subnormal. There was copious hæmorrhagic vomiting and the patient might talk naturally and remain conscious almost to the end.

Section of Obstetrics and Gynæcology.

President—Mr. VICTOR BONNEY, M.S.

[*February* 19, 1932.]

DISCUSSION ON GONORRHŒA AND OTHER CERVICAL DISCHARGES.

Colonel L. W. Harrison: In the time allotted to me I can only indicate some principles on which we might find a way out of the morass of uncertainty in which most of those who have the duty of treating vaginal discharges are struggling.

The present chaos is sufficiently indicated by the variety of treatments which one can find in a tour through the Venereal Disease Treatment Centres, and advocated in the literature, as also in the new remedies placed on the market almost weekly, each of them stated to be superior to its predecessors in power of penetration, bactericidal efficiency and kindness to the tissues. An example is the number of silver preparations, of which some time ago I collected the names of no less than forty-five.

In most clinics I have found the treatment of vaginal discharges to be that considered appropriate for gonorrhœa, and there seems to be comparatively little attempt to distinguish between discharges due to gonococci and those due to other causes. Commonly the treatment is by douching, with perhaps some half-hearted swabbing with protargol, practised at intervals of about a week and perhaps also, though much more rarely, the insertion of a medicated pessary.

I suggest here that more would be achieved by greater precision of diagnosis and by treatment which is more purposeful (in the sense of being directed to removal of the particular cause in the individual case) than is the common treatment blindly applied to all cases of vaginal discharge, as if they were of the same nature. In diagnosis I would supplement clinical examination by microscopic and cultural tests, and to these would add the complement-fixation test. Many are content with the microscopic test and think cultures superfluous. I can only say here that those who dispense with cultures are depriving themselves of a very useful means of diagnosis.

In a series of 225 consecutive cases of gonorrhœa in the female analysed by Dr. Clements and Dr. Payne in my clinic, the first examination revealed the gonococcus only by culture in 55. It was found at this examination in culture and smear in 81 cases, and in smear alone in 74, so that, but for the culture the organism would have been missed at the first examination, if not altogether, in an important

proportion of cases. As to the complement-fixation test, I am surprised that it is practised so little in this country. The evidence of its value in diagnosis, which has been produced in abundance by Thomson, by Osmond and Oliver, by Price and other workers in Great Britain and by sound men in other countries, ought to make those pathologists who doubt its reliability look to their technique.

With the help of the methods of diagnosis which are now available it should be possible in the individual case to decide fairly quickly if it belongs to one of three main categories into which for purposes of treatment I would divide most cases of vaginal discharge. The three are gonococcal, bacterial other than gonococcal, and chemical. Of the chemical cases I will say no more here than that many a vaginal discharge in a patient who has douched for years, or had her tissues tortured with chemicals, has been dried up by masterly inactivity. In cases of bacterial origin we ought to decide as early as we can whether the offending bacteria are gonococci or other organisms, because it seems to me that the principles of treatment of the two classes differ in some important respects.

In the non-gonococcal bacterial infection we are dealing with something more superficial, more accessible to bactericidal agents applied to the surface and therefore with a condition in which we can hope most from a properly directed frontal attack. In the gonococcal, on the other hand, we have an infection which is largely submucous, intra- and peri-glandular and altogether less accessible. In such a case we cannot rely on local treatment to do more than help drainage and detoxicate the discharges. Our main reliance must be on the patient's powers of resistance, which we must exploit to the utmost.

The proportion of non-gonococcal to other bacterial infections in cases of vaginal discharge must vary in the different clinics. In my own, Dr. Clements and Dr. Payne's analysis of 294 consecutive cases of vaginal discharge showed 142 to be gonococcal and 152 due to other bacteria. In the non-gonococcal the absence of gonococci was established by repeated smear and cultural examinations over periods averaging approximately three months. I am confident that large numbers of cases of vaginal discharge are wrongly diagnosed as gonorrhœal.

With regard to non-gonococcal infection, I think we might achieve more by greater precision of application of the remedies we employ and this with some regard to the length of time a chemical antiseptic requires to destroy bacteria, particularly when these are mixed with and protected by organic matter. How often do we see patients with cervical, non-gonococcal infections in which ordinary vaginal douches have been employed for months, though a little thought would convince the practitioner that the bacteria in the cervical canal cannot be affected by lotions swished round the vagina, often, too, in the lower reaches of this passage. How often do we see cervical infections treated with casual and momentary applications of some chemical in a strength and for a period which offer only the slightest hope of destroying the micro-organisms established there. On the other hand, we see also applications of silver nitrate in such concentrations as to destroy the mucous membrane and make it a beautiful incubating medium for the growth of organisms that reinvade it from the neighbouring, untouched recesses of the vagina. I suggest that we should be more likely to succeed in these non-gonococcal cases if, having decided on an antiseptic line of treatment, we first chose the chemical which seems to damage the tissues least, in a strength which when further diluted by the secretions already present in the canal, still remains bactericidal for the required length of time, and if we then apply it for as long as we can during each sitting to every part of the affected surface. My favourite antiseptic for non-gonococcal cervicitis is mercurochrome-220, because it seems to damage the tissues less than do other antiseptics. I apply it to the cervical canal on a urethroscopic swab-stick in a strength of 10 per cent. I leave it in contact as long as practicable during each sitting, changing the swab once or twice whilst painting every part of the vaginal

surface as thoroughly as possible with the same solution. I feel in doing this that from any part I might leave untreated, reinfection would start and that the lower the dose of reinfecting bacteria, the less likely they are to regain their original footing. I know the practical difficulties in carrying out such a line of treatment as frequently as is desirable, and in the dislike of patients to treatment with dyes, but in this matter we should adopt the procedure most likely to cure the patient and not an obviously useless form of treatment because the patient prefers it. I do not claim that antiseptic dyes are the best for our purpose. I plead only for the principle of using the best antiseptic we can find and of giving it a chance of doing its work, not imagining that it will be successful if just pushed anyhow in any sort of strength into—or somewhere in the neighbourhood of—the canal we wish to treat.

In gonorrhœa the problem is different. Local treatment is certainly necessary but it has strict limitations, and an equal or more important factor is the patient's resistance. Local treatment can do no more towards eradicating the disease than neutralize the toxins on the surface and promote drainage. To attempt to destroy gonococci buried in the depths of the tissues and in the glands opening on to them, by a frontal attack, is only to invite disappointment, and often enough the methods employed in pursuit of such a plan reduce the resistance of the tissues, besides making them a prey to invasion by the numerous organisms normally found leading a saprophytic existence in the vagina.

We are at present too much inclined to regard the factor of resistance as beyond our control. We are apt to think vaguely that it might be improved by a course of vaccines given blindly according to some dosage prescribed on general lines, and when the desired result has not been achieved by the traditional course of seven or eight injections of so-and-so's brew, we begin to think that vaccines are of no use in treating gonorrhœa. I suggest that a more rational way is to employ the complement-fixation test. I have been led to my views on the value of this test by observation of the work of Dr. David Thomson at Rochester Row during the European War and by recent work which Dr. Clements on the clinical side has been carrying out at St. Thomas's Hospital with a special vaccine made for him by Dr. Cliver on the principles elaborated by Dimond at the Royal Herbert Hospital, Woolwich, some years ago. The investigation of the effects of this vaccine has included, besides clinical observation, and microscopical and cultural tests, titrated complement-fixation tests carried out by Dr. Hughes in the laboratory of my Department.

I am sorry that Dr. Clements will not have an opportunity in this discussion of presenting his observations personally, and that I can here only give the gist of my own impressions derived from a study of his careful notes of the cases he has treated with this vaccine. They show a number of cases in which, previous to vaccine treatment, gonococci had persisted in the discharges for many months, in spite of careful and regular local treatment. At the same time the complement-fixation reaction had remained negative or only feeble. In these cases the local signs were usually only slight, as if the tissues had not the reactive power to turn the germs out. Then this form of vaccine treatment was instituted and in most cases had the effect of raising the titre of the complement-fixation reaction, with coincident disappearance of the gonococci. In some others the complement-fixation reaction was unaffected by this vaccine, and the gonococci also persisted. Dr. Clements's observations further show that there is a wide difference in the response of patients to the vaccine in other respects. In some a very small dose is followed by a smart local, general, and focal reaction whilst others tolerate a considerably larger dose with ease. The relation of clinical reaction to serological response has not yet been worked out sufficiently to enable any guiding rules to be formulated, but this work shows that vaccine treatment must be much more individual and more closely watched than is usual at present if we are to obtain full value from it. I judge then that in a case in which the disease persists and the complement-fixation reaction has not reached a

fairly high titre after some weeks, one thing which is indicated is to increase the resistance by administration of a vaccine and if one method of administration and one brand of vaccine fail to increase the titre of the complement-fixation reaction, we should try another. The titre may be raised and yet the gonococci persist; in that case we should ask if there is not some focus left undrained. Here I may say that the method of injecting the uterine cavity with glycerine, as elaborated by Hobbs, has often served us well. It is not difficult to accept the view that persistence of gonococci with a strong complement-fixation reaction is explicable by defective drainage when we think of the cases of the kind in the more easily observed male urethra where often enough the opening out of a peri-urethral infiltrate has brought the attack rapidly to an end. I think that if we guide our treatment of gonorrhœa on such principles, we are working on more certain lines than by relying only on the clinical appearances and the results of microscopical tests.

Dr. J. J. Abraham, dealing with the methods and results obtained at the Lock Hospital, said that of 1,000 consecutive cases of vaginal discharge, 152 were non-venereal, 848 were clinically gonorrhœa, and of these, 411 were proved by pathological tests to be gonococcal, leaving 437, i.e., 51·3%, negatives, although clinically gonorrhœa was suggested. 305 out of the 1,000 patients were pregnant on admission, and of these 259 were clinically due to gonorrhœa, although only 91 showed the gonococcus. These figures suggested that it was more difficult to isolate the gonococcus in pregnancy than in the non-pregnant patient. He then gave figures as to the relative frequency of various complications, such as salpingitis, arthritis, &c.

Dr. Abraham next discussed the criteria of cure, and confessed that the difficulties were very great, as even a number of negative gonococcal reports could not be taken as evidence of cure. The tests he relied on were that all clinical evidence of the disease should be absent from the urethra, Skene's and Bartholin's glands, the vaginal orifice, the anus, and the cervix. The uterus and tubes on bimanual examination should be free from inflammatory signs. Smears and cultures from the urethra, Skene's and Bartholin's glands, the cervix, and anus should be negative. These tests should be taken two days before menstruation, and two days after its cessation, and twenty-four hours after a provocative injection of gonococcal proteose. Finally, cultural examination of the urine should be made from a three- or four-hours-old specimen. Dr. Abraham said that he had, with reluctance, come to the conclusion that the complement-fixation test was not reliable. [He then discussed the treatment under various headings.]

Dr. Anwyl Davies said that the great difficulty in treating these cases was to reach the infecting organism in the tissues, and to raise the resistance of those tissues. In some experiments that he had carried out with the late Professor Shattock, he found that silver nitrate and picric acid only penetrated 1/16th in. beneath the mucous membrane of the cervical canal, and that these drugs caused the formation of a tough plaque of dead epithelium which blocked the mouth of the glands and prevented drainage, with the result that the organisms had a perfect medium and temperature to grow in. He considered that mercurochrome was of some value in vulvo-vaginitis in children aged under two years and a half. He criticized the local treatment of the urethra and cervix without also treating the body of the uterus, which, in his opinion, was very often infected. If this was not true, it was difficult to account for the high percentage of boggy tender uteri. His experience of diathermy was very unsatisfactory. Although the gonococcus was so easily killed *in vitro* at 160° F., in the body it was not destroyed by any temperature which left the tissues intact. Experiments proved that diathermy reaching a temperature of 112° F. to 114° F. in the cervical canal, administered even for thirty to forty minutes each time twice weekly, failed to knock out the gonococcus. If we

believed diathermy to act by heat, it was obvious that a short way away from the electrode the temperature was very little above that of the body, thus creating an optimum temperature for the growth of gonococci. He was not favourably impressed by vaccine treatment. Protein shock lowered the immunity of the tissues to the gonococcus. He considered that glycerine was the best bactericidal substance to use, as it was antiseptic and hygroscopic ; it was also bland, non-irritating and odourless. [Dr. Anwyl Davies then went on to give the routine examination carried out at the Whitechapel Clinic, and showed charts on the screen which indicated the careful way in which the patients were looked after.]

Dr. Lynette Hemmant said that she had worked in five separate clinics, and was convinced that the first great difficulty that confronted them was one of diagnosis, and this was the reason why it was so difficult to stamp out the disease. She described some special cultural methods evolved by Orpwood Price, by which colonies of gonococci could be quickly differentiated from other organisms. She laid great stress on the importance of the psychological encouragement of the patients, as so many of them took up the hopeless attitude that the disease was incurable.

Dr. D. Lees: The proportion of patients who complain of a vaginal discharge and in whom the gonococcus is isolated is not so important as the elimination of gonorrhœa as the cause of the discharge. This can only be ascertained accurately by a careful clinical examination, supplemented by bacteriological tests of specimens taken from the urethra, cervix, and Bartholinian ducts.

If the clinical picture suggests a gonococcal infection but the bacteriological tests do not confirm this, these tests should be repeated at a later date and under more favourable conditions when the patient has a full bladder and has not douched for a day or two previous to examination. Specimens taken just after a menstrual period are of more value still both in diagnosis and in tests of cure.

It should not be necessary to emphasize that a differential stain is always desirable, and of those in common use I prefer that of Kopeloff and Biermann because the decolorizing of the film is more accurate and less expensive with acetone than with alcohol, and there is not the risk of over decolorizing or the reverse as there is in Jensen's Modification of Gram's Iodine Stain.

We may divide adult patients coming to hospital complaining of vaginal discharge into three large groups :—

(*a*) Those who are frankly gonorrhœal.
(*b*) Those in whom the clinical condition and the history strongly suggest this, but in whom there is not definite bacteriological evidence.
(*c*) Those in whom the discharge is definitely not due to a gonococcal infection.

The management of these three groups depends largely on the available hospital facilities. If the V.D. clinic is situated in a general hospital the first two groups can be treated more conveniently in V.D. wards.

In the third group I think it is important that the patient should be transferred from the V.D. clinic to the gynæcological unit at once so that no stigma may be attached to her ; gonococcal infection in the female patient differs little in symptomatology and signs of disease from infections due to other organisms, and it is obviously unfair to many married women to segregate them as cases of venereal disease.

In Edinburgh we adopt this method, except in cases of pregnancy (these are transferred to the Maternity Hospital in which the rooms for treating patients suffering from any antenatal discharge are an integral routine of the department). It would be of advantage to the patients, and a step in the right direction, if the same principles were applied to non-gravid cases in general hospitals. It would obviate many of the social difficulties which we have to contend with at present and

materially lessen the number of patients who cease attending hospital before they are tested for cure.

In clinical diagnosis we must use the sense of sight as opposed to the sense of touch, and appreciate that a single negative examination does not eliminate the existence of a latent gonococcal infection.

In the treatment of gonoccal infections it is difficult to dogmatize except on general principles. The fundamental principles are :—

(1) The promotion in every possible way of the natural resistance of the patient, by physical and mental rest, by attention to elimination by the bowel, kidney, skin, by habits of life, etc.

(2) The establishment of good drainage from the infected parts, and the keeping of the parts in a clean and dry condition.

(3) The destruction of the infecting organism locally, by the application of antiseptics or other methods.

(4) The stimulation of the patient's resistance by the administration of vaccines, proteins or sera.

I will refer briefly to the two latter methods only.

Local antiseptic treatment has its limitations in female infections in that the antiseptic cannot be brought into touch with many of the infected areas, such as the racemose glands of the cervix, and the depths of the urethral crypts.

Each worker has his own particular choice of antiseptic. I do not favour the application of strong solutions either to the urethra, the cervix, or the vagina ; their strength does not increase their penetrability and often damages the epithelial covering. I feel certain also that it is advisable to change the antiseptic after using it for from seven to ten days, and that more is to be gained, especially in bladder lavage and douching, by increasing the temperature of the antiseptic than by increasing its strength.

The antiseptics for which I have preference are potassium permanganate, 1/6000 for the urethra and bladder, and picric acid, 1% in glycerine, for the cervix. As alternatives for urethral irrigation, albargin, 1/6000, or chloramine T. 1/5000 are clean and effective preparations. As an alternative to 1 % picric acid in glycerine for the cervix, I use a solution of equal parts of iodine and alcohol in glycerine or 1% mercurochrome in glycerine. In my experience the dye preparations are not any more effective than many cheaper preparations, and they have the disadvantage that patients object to the staining of their clothing.

There are few cases of acute, subacute and chronic gonorrhœa in which douching has any advantage and I prefer in every case moist swabbing of the vagina through a fenestrated speculum ; exception must be made in acute and subacute tuba infections, in which a warm vaginal douche of at least four pints helps to bring about resolution of the inflammatory process.

While daily treatment or treatment on alternate days is advisable in all acute cases, it is not always possible for the patient to attend for this, and in such cases a douche may be used for cleanliness and the patient may be instructed in the insertion of a medicated pessary into the urethra. Chloretone is added to all medicated pessaries on account of its anæsthetic action. The all-important point in treatment is the meticulous care with which it is applied to every infected area in each individual case. Concomitant with this treatment it is important to rest the patient in acute cases until after the first unwell period subsequent to the infection. In the resolving stages and in chronic cases, drainage from the infected areas must be improved by such measures as suction of the urethra and cervix, or the passage of a sound into the urethra. These measures open up the submucous tissues and promote drainage, and assist materially in preventing the establishment of chronic foci of infection surrounded by fibrous tissue.

In the treatment of Bartholinian infections, if they are acute or subacute I have found nothing more effective than aspiration of the abscess and the injection into the gland cavity of 1 to 2 c.c. of electrargol. In any case which does not react to this form of treatment, excision is undoubtedly the best method to adopt.

Many forms of adjuvant treatment have been tried. I have found that the careful administration of a good antigenic vaccine assists in lessening the virulence of the infection and in preventing complications; of itself it is not a cure. The same doses will not suit every individual and the vaccine must be given intelligently in the light of the effect it has produced on the local and general condition of the patient.

I have tried many other forms of treatment which have been advocated from time to time, among them the following:—The application of a vaccine to the infected area by spraying as advocated by Besredka. Neither in adults, in cases of pregnancy, nor in children suffering from vulvo-vaginitis, did this method give promising results. Our experience with the application of a gonococcal antivirus was similar. I have also tried the application of a bacteriophage as suggested by d'Herelle, and with the exception of cases of ophthalmia the gonococcal bacteriophage did not give any results. Lactic acid in a saccharose base has given no better results, and in the case of vulvo-vaginitis I have washed out the infected area with sterile milk and then placed in the vagina a pure culture of *Bacillus bulgaricus*; the results were far from favourable.

More recently we have been trying the effect of applying a filtrate of a broth culture of a *Staphylococcus albus* which has always proved inimicable to the gonococcus *in vitro*; even when applied twice daily to the infected urethral and cervical surface, this filtrate appears to have little, if any, influence on the gonococcus.

Many antiseptics which are stated to have the power of penetrating living tissues fail to influence the infection as promised by their protagonists. A preparation known as citragan which has been used freely in Denmark, was very carefully tried and the results were favourable up to a point, but not any more so than with picric acid and other antiseptics.

We must recognize that antiseptics have definite limitations, and unless they can be brought into touch with the gonococcus they will not eradicate the disease.

Diathermy has not given the promising results which were anticipated from this form of treatment; it is an adjuvant and nothing more.

I do not mean you to assume from what I have said that gonorrhœa is not curable; with care and perseverance every case can be cured and we should always adopt a reasonable optimism when asked by patients for a prognosis. Gynæcologists are inclined to take a pessimistic view of this, just as neurologists do in syphilis, because they see only the failures and judge accordingly.

When I am asked to define the criteria of cure, I must admit that this is difficult, but the following must be fulfilled before any female patient can be considered free from gonorrhœa:—

(1) Absence of clinical symptoms and signs of disease for at least one month after cessation from treatment.

(2) Absence of any bacteriological evidence of gonorrhœa during the same period.

(3) Repetition of bacteriological tests of secretion from the urethra, cervix and Bartholinian ducts taken after two successive menstrual periods after apparent clinical cure.

(4) At one of the previous tests it is important to administer a provocative injection of polyvalent gonococcal vaccine (300 mil.) thirty-six hours prior to taking the specimes. It enhances the value of the tests if a plug of gauze soaked in glycerine is inserted into the cervix the previous day.

(5) Bimanual examination of the pelvic contents to ascertain that there is no cellulitis or involvement of the Fallopian tubes.

(6) Urethroscopic examination to eliminate the presence of soft infiltrates and infection of Skene's ducts.

(7) This observation and testing over a period of three months after apparent cure, enables us to tell the patient that she is provisionally free from infection.

(8) A similar clinical and bacteriological examination should be made three months later just subsequent to a menstrual period. It may be supplemented by testing the blood by the complement-fixation test, which at that date should give a negative result.

If there is no evidence of disease at this examination, the patient can be considered free from infection.

There is one aspect of this question which has impressed me. In the treatment during pregnancy of vaginal discharges which one has not been able to prove due to gonorrhœa, a careful antenatal toilet carried out two or three times weekly by moist swabbing the vulva and vagina and by topical applications to the cervix followed by dusting the parts with an absorbent powder such as dermatol gives excellent results. In addition, when these cases are examined post-natally the clinical condition of the cervix and vagina is generally very much better than is found in patients who have had no antenatal treatment. This is the considered opinion of my obstetrical colleagues who see these cases post-natally. There is a further fact which has emerged from our ante-natal treatment of pregnant women : the puerperium of such patients is less morbid and there are fewer complications during it than in the so-called clean cases which are dealt with in the other wards of the hospital. This, of itself, is a striking argument in favour of antenatal treatment of vaginal discharges, as opposed to the attitude of masterly inactivity which is practised and advocated by quite a number of obstetricians.

Dr. D. H. MacLeod : The clinic at the Middlesex Hospital for the treatment of gonorrhœa and other vaginal discharges has been in existence since 1917.

Methods of treatment are legion, as in all conditions for which there is no specific cure. Routine irrigation has been the principal means adopted at this clinic and up to the present it is attended with as good results as—or rather with no worse results—than any other. The irrigation is carried out by a competent nurse under the supervision of the medical officer in charge. The basis of this treatment, briefly, is the irrigation of the urethral and cervical canals with a solution of sodium bicarbonate to remove the excess of mucus, followed by a 10% solution of dichloramine T. The vagina is then swabbed dry and lightly packed with gauze soaked in a 2% solution of mercurochrome in glycerine, which the patient is instructed to remove the following morning and to burn. Patients attend daily for the first month of treatment or as advised by the medical officer according to the severity of the symptoms.

All subacute and chronic cases are treated on the above lines. Cases with acute symptoms are uncommon at the clinic. In such cases the patients are sent to bed and ordered frequent hot baths until the acute symptoms have subsided, when routine irrigation treatment can be carried out.

Patients who are pregnant receive urethral irrigations as above and the cervix is painted twice a week with Bonney's blue, which is a $\frac{1}{2}$% solution of both crystal violet and brilliant green in alcohol, or with a 10% solution of protargol. The vagina is not packed.

The patients are seen by the medical officer in charge at the end of every menstrual period and before resuming treatment. Smears are taken from the urethral and cervical canals and the gonococcus is more likely to be found then than at any other time. Erosions of the cervix are painted with iodized-phenol or cauterized with the actual cautery ; they respond but slowly to treatment. Obstinate urethritis often responds to applications of a 10% solution of argyrol.

The gonococcus, lying as it does, deep down in the intricate branchings of the cervical glands, must theoretically be beyond the reach of any kind of local treatment and nothing short of hysterectomy can remove it. We believe, however, that the infection, in time, wears itself out, or is finally overcome by the active resistance of the patient. Irrigation treatment, by keeping the patient clean, prevents reinfection and encourages the flow of healthy secretion. Care of the general health and increasing the defensive mechanism of the tissues by the administration of special remedies such as radiostoleum, will do much towards hastening a cure.

Vaccine treatment.—During the year 1931, thirteen cases were treated with gonococcal vaccines. Nine of these were admitted during 1930. By the end of 1931, twelve were still attending for treatment, and, of these, nine were clinically positive. Only one case was discharged as cured. We are not convinced from these results that much benefit was derived from vaccine treatment in our cases.

The question of cure and diagnosis.—Before a patient is cured, both clinical examination and examination of film preparations are taken into account. Clinical examinations are said to be negative if there is no discharge or any macroscopic evidence of disease. Film preparations are negative if the gonococcus is absent and the pus cell count is less than 50% of the total cell count. A patient is considered cured when both clinical and microscopical examinations are negative on three successive occasions at monthly intervals. The smears should be taken immediately after the cessation of a monthly flow and before resuming treatment, for the gonococcus is most likely to be found at this time. The necessity of corroboration between both examinations is borne out by the frequent occurrence of gonococci in smears from those patients which appear to be clinically negative. On the other hand cases which have copious discharge may not uncommonly show negative smears.

The gonococcus is very elusive and may only be found after several examinations, but it is noticed that in these cases the pus cell content is usually over 50%. Many cases, though at first appearing to be non-specific in nature, eventually turn out to be gonococcal.

Summary.

(1) The main obstacle towards the cure of gonorrhœa among patients attending the clinic at the Middlesex Hospital is the protracted nature of the treatment.

(2) We have met with little success with the use of gonococcal vaccines.

(3) The average duration of treatment among the patients discharged as cured was as long as 15 months.

(4) The duration of symptoms before the commencement of treatment appeared to bear some relation to the cure rate among gonococcal infections.

(5) Cases with gonococcal urethritis only, appeared to stand a better chance of cure than cervical infections.

(6) Acute cases of gonorrhœal infection were rarely seen.

(7) Clinical examination of a patient was found to be often unreliable. Gonococci were found in patients who had no clinical evidence of the disease.

(8) In several cases gonococci continued to appear in films as long as 20 months after the onset of treatment.

(9) Rectal infection appeared to be uncommon and was not responsible for the continued appearance of the gonococcus in the vaginal discharge.

(10) We did not find that tubal inflammation was a common complication among the patients attending the clinic.

(11) Thirteen per cent. of the total admissions during 1930 were discharged as cured by the end of 1931. Of the cases with gonococcal infection 21 per cent. were cured, whereas of those with non-gonococcal infection only 6 per cent. were cured.

Dr. Chassar Moir : I shall confine my remarks to some points concerning the treatment of gonorrhœa, and of vaginitis of other origin.

I feel that it is necessary to emphasize the futility of attempting to compare statistically the results of treatments by different workers. Gonorrhœa quickly becomes a chronic disease, and there is no certain way of determining when it ceases to exist, neither can it be said with certainty when a patient ceases to be infectious. A patient may receive a certain treatment from Dr. A and be discharged in, say, four months' time, while a similar patient receiving treatment from Dr. B may not be discharged for a year or more. It does not necessarily follow that Dr. A's treatment is better than Dr. B's; it may mean that Dr. B is a more cautious man than Dr. A. The bacteriologist's reports do not overcome this difficulty, even if a rule is made to examine only post-menstrual smears. One bacteriologist, seeing a suspicious Gram-negative diplococcus, may rightly report that gonococci are still present, while another, looking at a similar slide, may consider that there is nothing diagnostic in that single diplococcus, and may report that no definite gonococci are seen.

For these reasons I feel that there is nothing to be gained by comparison of methods unless these methods are tried by the same doctor and are used for the same class of patient. I shall, therefore, not give more than a very few statistics. I can, however, give my impressions of the results of routine treatment with local applications, and contrast them with the results obtained by diathermy of the urethra and cervix. Any value which this comparison may have lies in the fact that with very few exceptions I have personally examined each patient from the time of her first visit, and have myself carried out each of the treatments by both methods.

About two years ago I visited Dr. Cumberbatch at St. Bartholomew's Hospital, and he and his assistant, Dr. Simon, kindly demonstrated the details of the method used in the electrical department of that hospital. I have since used the same technique in the V.D. Clinic of University College Hospital. I have found that it is safe to use a heavier current in both the urethra and cervix than is said to be possible in Cumberbatch and Robinson's textbook; this, however, may be due to a peculiarity of the particular diathermy machine or recording meter which I use.

In all, I have treated with diathermy 44 patients who had definite gonorrhœa. Most of these patients had previously been treated by local antiseptic applications until the disease had reached the chronic stage. The standard number of diathermy treatments was six, and they were given at weekly intervals. All treatment was then stopped and a series of monthly postmenstrual smears were taken.

Of the 44 cases, 20 were clinically cured, and showed three or more negative postmenstrual smears. Sixteen cases did not report back sufficiently often to obtain more than one or two such smears, and four did not report at all after the course of diathermy. Most of these patients who ceased to report were clinically cured, and I believe that almost all of them were satisfied with their condition, and therefore did not trouble to attend as requested. Three cases showed positive smears after the course of treatment. One of the patients was in all probability re-infected by her husband, who had returned to live with her. One case was apparently cured, but returned four months later with a Bartholin gland abscure. The urethra and cervix remained healthy, and smears from them were negative, but pus from the abscess contained the gonococcus.

Were I strongly biased in favour of diathermy I would claim that I had quickly cured a large percentage of my patients. I prefer, however, to be much more

critical. Most of these patients had already received from three to five months' regular local treatment, and the diathermy was used in the chronic stage when positive smears were difficult to obtain. Moreover, many of the patients did not attend sufficiently often to enable a definite statement on the bacteriological condition of the cervix and urethra to be made. On the other hand, there were several patients who had responded badly to ordinary treatment, and who had continued to yield positive smears for many months or even years. After diathermy these patients were apparently cured when judged by clinical and bacteriological evidence. I might quote the case of one unfortunate girl who had received regular twice-weekly local treatment for more than two years. On the 243rd visit gonococci were still present. (This patient had also had several hundred intermediate treatments with douches.) After a course of diathermy she was clinically cured and five smears taken at monthly intervals were examined with negative results.

How does diathermy act? The claim that the heat generated in the tissues directly destroys the gonococcus cannot be upheld. I have carried out the experiment of taking a culture from the urethra in cases of acute gonorrhœa, before diathermy and again directly after diathermy treatment. Just as many gonococci were grown in the one culture as in the other. I believe that diathermy acts by promoting drainage, and by increasing the vascularity of the parts treated. I have frequently noticed that although the cervix has been wiped dry before treatment a copious mucous discharge is present after treatment; moreover the cervix becomes soft and vascular, not unlike the cervix of early pregnancy. This activity of the glands must wash out retained organisms, and the induced vascularity doubtless increases the local metabolism and presumably stimulates the formation of local immunity. If these conjectures be true, it follows that it is irrational to use diathermy in the acute case. Clinical experience confirms this, and I have found that diathermy produces no benefit in such cases and may in fact aggravate the disease. Two of my patients (not mentioned in previous figures) developed acute salpingitis, and in one case an acute Bartholin gland abscess followed on the treatment. I now never use diathermy in an early case of gonorrhœa.

The opinions which I have formed regarding treatment of cases of gonorrhœa in the female with, on the one hand, local irrigations, foam-producing pessaries in the cervix and urethra, applications with various antiseptics such as flavine in glycerine, and, on the other hand, diathermy of the cervix and urethra, are these:—

(1) That with the local applications about 50% patients are clinically cured and cease to yield gonococcus after five or six months' intensive treatment.

(2) That in the remaining 50% it is a waste of time, both of doctor and patient, to continue longer with such treatment.

(3) That those cases which do not quickly clear up are best treated by diathermy.

(4) That diathermy has no specific action in killing the gonococcus, but that it does promote drainage and probably stimulates the local resistance to infection.

(5) That many chronic cases will apparently clear up after a course of diathermy treatment.

Before concluding I will mention another class of case. I refer to a certain type of severe leucorrhœa which might aptly be termed non-gonoccocal gonorrhœa. These patients suffer from a profuse irritating vaginal discharge, sometimes of sudden onset. In the unmarried patient there is probably no history of coitus; the hymen may be intact. In the married patient there is no history of urethral discharge in the husband. Local examination does not show the tell-tale signs of gonorrhœa such as pus in the urethra, enlarged Bartholin's glands, or endocervicitis; the urethra and cervix are healthy, and the cervical canal often shows the normal glistening plug of mucus. There is, however, a very definite general vaginitis. The surface of the vagina is bright red and congested and in extreme cases it has a granular appearance. The portio shares in the vaginitis.

During the last six months I have examined the vaginal secretion of sixteen such patients and I have found the flagellated protozoal parasite, the *Trichomonas vaginalis* in each case; sometimes it is present in enormous numbers. Included in this group are a few patients who had genuine gonorrhœa and who had been treated with apparent success, but who still complained of a slight leucorrhœa. Many of these patients had a slight general vaginitis, and they also were found to harbour the *Trichomonas vaginalis*. It has been said that the trichomonas is harmless, and that it is found in cases of leucorrhœa simply because the increased moisture of the vagina favours its growth. To obtain some information on this matter I have examined the secretion of thirty cases of acute gonorrhœa and I have failed to find the organism. I have also examined the secretion of thirty normal pregnant women with negative results. I am aware that many workers have found that the *Trichomonas vaginalis* is a relatively common parasite, and that some statistics have put its presence as high as 13% or more. It is not clear, however, whether the patients examined did not include cases of leucorrhœa of the type to which I wish to draw attention. In view of the constant finding of the trichomonas in association with the characteristic vaginitis, it seems reasonable to suppose that these protozoa are the cause of the inflammation.

Treatment of such cases is difficult and may indeed cause much more trouble than the treatment of genuine gonorrhœa. The Lassar's paste method which has been advocated by American workers has not proved in my hands to be of any value. A more satisfactory line of treatment is a daily painting of the vagina with a 1% solution of picric acid in one part of spirit and three of water. This is carried out for a fortnight, and is followed by daily douching with 1% lactic acid solution.

Dr. David Watson (Glasgow):[1] I propose to limit my remarks to the bacteriology and treatment of endocervicitis, and to concentrate on such points in my own procedure as may not be known to you, although I have been teaching them for several years.

Bacteriology.—Gonococcal disease can only be diagnosed with real accuracy by finding typical specimens of the organism. At one time, when I personally made and examined the smears, I thought everything depended upon the method by which they were taken, but since a special bacteriological department has been organized at the Lock Hospital in Glasgow I have learned that the bacteriologist's view may differ from the clinician's, and it was only after a period of comparative failure to be of use to the clinical side that the bacteriologist was persuaded to give returns bearing the words "positive for g—c Watson." This means that there has been found in the smear, isolated pairs of coffee-bean-shaped Gram-negative diplococci of the right size. Of course when clumps are found intracellularly a positive report, without reservation, is furnished.

The method of taking specimens upon which I insist is that after displaying and cleansing the cervix the cervical canal has to be freed of its contents and as a rule several wool-wrapped probes are required for this purpose. Sometimes additional methods are necessary, such as swabbing the cervix with 1 in 5 caustic potash solution or ricinoleate of soda, or expression with cervix forceps. A wool-wrapped probe is finally used for making the smear. What is wanted is recent secretion expressed from the cervical glands, and for this purpose pressure is made on the walls of the cleansed canal by the rotating probe.

Specimens taken in this way will rarely show any intracellular clumps, but will show typical Gram-negative kidney-shaped diplococci in many cases in which otherwise it might be impossible to identify the gonococcus, e.g., in smears made from a loopful of old cervical discharge perhaps crowded with saprophytes. Experience has taught me that when smears are carefully taken as described, I can place considerable

[1] Taken as read.

reliance on the results; thus the presence or absence of infectivity is indicated, the mode of treatment is influenced, and one of the criteria of cure is furnished.

Treatment.—I am not aware of any systemic treatment which can be relied on to hasten cure, although, incidentally, I may mention that recently I saw a nurse just returned after a year's residence in a malarial country where she had been liberally dosed with quinine, who attributed the cure of an intractible endocervicitis to this drug, and with this opinion I quite agreed. I rely then on local treatment. When a patient comes under treatment she is swabbed on the first occasion with 1 in 2,000 biniodide of mercury followed by 1 in 200 lactic acid, and on the later occasions with lactic acid alone, and the last item in all treatment is the insertion into the posterior fornix of a small pessary consisting of lactose and an active culture of lactic acid bacilli.

When continuance of an infected condition of the cervix is shown by persistence of gonococci in the smears and discharge from the cervix, I have several preparations at hand for local application, these include: dichloramine-T in chlorcosane; eucalyptus and castor oil; formaline in glycerine; iodoform in aniline oil; and quinine in powder and in solution; an antiseptic dusting powder in an insufflator; an antiseptic and sedative ointment.

All of these are in occasional use, but the preparation which is mainly used, and is almost a matter of routine, is 5% acriflavine. It is dissolved in a sufficiency of glycerine and then mixed with an emulsion of castor oil so as to make a 5% suspension of the acriflavine. It may be objected that a 5% solution of acriflavine as it precipitates protein will be rendered inert as a penetrating antiseptic, but I have proved that this coagulum is soluble in excess of the albuminous fluid, therefore it still remains active in the conditions of hypersecretion and exudation obtaining within the inflamed cervical canal. Solution of the coagulum proceeds until it is all dissolved and a continued action is thus maintained for some days. Application twice per week therefore is sufficient. This preparation is quite unirritating, on the contrary it is surprising how the appearance of an irritated granular cervix is seen to have improved even immediately after a treatment, in contradistinction to the increase in, or production of, granular areas and ectropion which follow caustic applications.

Method of application.—One of the principles upon which I lay great stress is that no solid instrument, such as a probe or sound, shall be passed into the uterus and the same applies, although perhaps with somewhat reduced force, to the cervical canal. Only tubular probes or sounds are used either for cleansing, for taking smears, or for making applications. My point is that ahead of the moist wool-wrapped probe, which in many cases will entirely block the external os, there is bound to be an increase of pressure, an increase which may force infected material through the internal os, or where intra-uterine instrumentation is being applied, through the openings into the Fallopian tubes. The alternative to probes is a hollow sound through which the antiseptic can be injected.

Dr. Margaret Rorke said that in her clinic at the Royal Free Hospital there were a great number of unmarried girls from Rescue Homes, and other non-pregnant single women, who were suspected of possible venereal disease. For this reason a large percentage of the patients proved to be suffering from vaginal discharge due to causes other than gonococcus. Dr. Rorke dealt largely with the treatment of vaginal discharges due to *Bacillus coli* and other infections. As a criterion of cure she suggested absence of signs and symptoms and three films negative to gonococci and free from pus. Tests were made after three different menstrual periods. A culture was taken thirty-five hours after a provocative injection of gonococcal vaccine. In some cases more humane provocative tests were made by giving cocktails or champagne, the cultures being taken the morning after.

Dr. Muriel Keyes quoted an interesting case in which diathermy applied on account of the genito-urinary infection caused great benefit in arthritis due to gonorrhœa.

Dr. D. C. Logan said that when she was working at King's College Hospital she had made it a rule to watch patients for two years after cessation of treatment, before discharging them as cured.

Section of Ophthalmology.

President—Mr. ELMORE W. BREWERTON, F.R.C.S.

[*January* 8, 1932.]

Double Optic Atrophy and Monocular Vertical Nystagmus (Left).—L. H. SAVIN, F.R.C.S. (for J. M. BICKERTON, F.R.C.S).

F. F., female, aged 26.

Left visual field obliterated except for a small temporal remnant. Right visual field slightly contracted peripherally. Vision: Right eye, $\frac{6}{24}$; with $+ 0{\cdot}5 = \frac{6}{24}$. Left eye, hand movements. The left eye shows a slow vertical nystagmus.

Wassermann reaction negative. Urine normal.

Implantation Cyst of Iris following Cataract Extraction.—R. AFFLECK GREEVES, F.R.C.S.

Extraction May, 1926. Cyst only noticed three months ago. It has been punctured since then by the surgeon who originally operated but has refilled, and the case was sent to me for opinions as to the treatment of the cyst and iris prolapse.

Discussion.—The PRESIDENT said that an upward section to include the prolapsed iris would be the most favourable line of treatment.

Mr. J. HERBERT FISHER said that if this were his case he would deal with it in two stages. It would not be difficult to raise a flap of conjunctiva over the prolapse, and after cutting off the knuckle of uveal tissue level with the sclerotic, or burning it off with the cautery, to replace the conjunctival flap. This procedure might result in collapse of the cyst, but it would probably refill, when a subsequent section would enable the surgeon to seize some of the cyst wall and withdraw it from the anterior chamber.

About twenty years ago he had had a patient, a boy, aged 17, who had been hit by a screw, which penetrated the globe close to the limbus in the 12 o'clock position. The iris was prolapsed, and he (the speaker) had performed an ordinary iridectomy with satisfactory results. Later the patient served in the European war, and returned from France with an implantation cyst at the bottom of the anterior chamber. He (Mr. Fisher) punctured the cyst but it refilled in a few months' time. He made a further section, and as the cyst was adherent to the iris tissue in which it was implanted, he was able, by performing iridectomy downwards, to remove the greater portion of the cyst wall. A pillar of the iris in the downward iridectomy prolapsed, and he had to deal with that in the way he was suggesting that Mr. Greeves should deal with the prolapse in this case. In his own case there was a sound scar. There were elements of the cyst wall left in the bottom of the anterior chamber, but they never developed into a further cyst. He could not now say whether the cyst wall was microscopic, but obviously the case was one of implantation cyst, and there was no cilium in the anterior chamber. Subsequently his patient had a good deal of astigmatism, because he had had iridectomy both upwards and downwards, but he still had $\frac{6}{9}$ vision with cylinder correction, and was carrying out his duties as an Army officer.

Severe Pannus of the Cornea. ? Trachoma. Case previously shown (November, 1927.)—HUMPHREY NEAME, F.R.C.S.

B. R., female, aged 18.

History.—1921. Attended Royal London Ophthalmic Hospital. There was a white opaque patch along the upper margin of the right cornea.

1925. Left cornea showed yellowish translucent area, non-staining. Chronic blepharo-conjunctivitis.

1927. The right corneal opacity was superficial and irregular, near the margin of the cornea. ? Hyaline degeneration. The left dense yellowish opacity had an irregular surface.

November, 1931. Both upper palpebral conjunctivæ showed fine papillary change, with mottling and irregular swelling of the surface, but no definite

granulations. The left pannus had advanced so as to obscure the greater part of the pupil (undilated). Both affected areas of the cornea were vascularized with superficial vessels.

The interest lies in the slow development of vascular pannus of the cornea, with marked slowly advancing opacity during six or more years.

Discussion.—Mr. A. F. MACCALLAN said that the conjunctiva of both upper lids showed the effect of treatment, and he considered the condition to be one of trachoma, stage Tr. III. The cornea in the right eye showed pannus, vascular tissue extending from the superficial vessels into the clear tissue of the cornea. On seeing the right eye only, he would say it was trachoma. The condition of the left cornea was somewhat anomalous; he had not seen such a condition previously.

Mr. FOSTER MOORE said he did not think that the condition was trachoma, as he had seen the patient when it first began in the right eye, the left eye then being normal. There was a yellowish epaulette-like invasion of the surface of the cornea above, with no involvement of the conjunctiva whether ocular or palpebral, and no pannus, and this disappeared rapidly, completely and spontaneously. There was no similarity to trachoma in any way. Certain remains of vessels resulted from the yellowish mass.

He had not examined the left eye except to observe that the corneal condition clearly was similar to what that in the right had been, and consequently he did not believe that that in the left was trachoma. There had no doubt been enough of local treatment to cause a red and swollen condition of the palpebral conjunctiva and so help to simulate trachoma.

Mr. J. HERBERT FISHER said that though the pannus was exceptionally dense in the left eye, there was now no room for doubt that the case was one of trachoma. Another feature which struck him was that the patient presented the appearance of a congenital syphilitic; there was loss of the septum of the nose, and there was a decidedly saddle-shaped bridge. The Wassermann reaction was negative, but there was not conclusive evidence that the case was non-syphilitic. He asked younger Members not to rely entirely on the result of the Wassermann, even when it was positive, and certainly not when it was negative. No information was supplied as to whether her mother experienced antecedent miscarriages, or deaths of children in infancy, or whether the patient had nodes on the tibiæ, Hutchinson's teeth, perforated palate, or faucial scarring; whether the parents were living, or, if dead, what was the cause of death; whether her father was the subject of locomotor ataxy or in an asylum with G.P.I. All those things were ignored and held to be ruled out by the negative Wassermann reaction!

A Demonstration of the Structure of the Lateral Eyes of the Adult Sphenodon.

By IDA MANN, F.R.C.S.

THE Tuatera (*Sphenodon punctatus*) is the only extant representative of the third order of reptiles, the Rhincocephalia. It occupies an intermediate position between tortoises and crocodiles on the one hand and lizards and snakes on the other. It is rapidly becoming extinct and at the present time is only to be found in a few small islets off the coast of New Zealand. It therefore seems desirable to put on record some observations which I have had the opportunity of making on a living specimen and on sections of the adult eye.

The specimen I examined had a total length of 44 cm. from the snout to the tip of the tail. The head was 8·5 cm. long, the body 17·5 cm. The skin is of a greenish mud colour and is covered with small tubercles and scales. There is a low crest extending from the neck to the tip of the tail. There are no external ears. The eyes are placed laterally, the angle between the optic axes being 160° or more. On the top of the head is a raised spot of a lighter colour marking the site of the parietal eye. This becomes obscured or converted into a depression with age. The organ is covered with skin and cannot be seen except on dissection.

The lateral eyes are provided with thick movable lids covered with greenish-brown scales. The palpebral aperture is 13 mm. from side to side and, when the eye is open, 4 mm. from above downwards at its widest part. Since the diameter of the cornea is 5 mm., or slightly more, it follows that the upper and lower corneo-scleral junction is never exposed and the iris is never seen complete. At the inner and outer canthus a triangular area of ocular conjunctiva is exposed. This is pale green in colour and is covered with fine capillaries having pale brown walls. The pupil reacts well to direct illumination, changing from a circle to a vertical slit. There does not appear to be any consensual reaction.

Appearances seen by focal illumination.—The cornea was extremely transparent and completely avascular. Practically no structures could be made out in it. The deepest layer of the iris stroma is a shining silvery buff, but this is only visible in a few very small patches, as it is mostly overlaid by splashes of a rich coppery-red metallic pigment, which is in turn obscured in some places by a superficial layer of thin chocolate-coloured tissue. The vessels all stand up from this layer in high relief, which becomes more marked towards the pupil, where many of the loops project almost perpendicularly from the surface of the iris. The walls of the vessels are densely coated with chocolate pigment, mixed here and there with the copper pigment of the stroma. No individual pigment cells are distinguishable nor is the direction of the circulating blood or its colour anywhere seen.

The vessels.—These are all roughly of the same calibre, no distinction being possible between arteries, veins and capillaries. At the margin of the pupil is a narrow, flat, dark brown zone, which appears to be avascular. Peripheral to this is an anastomotic arcade of large irregular vascular loops, fed by a network of vessels covering the rest of the iris. These vessels, though anastomosing freely, run for the most part a course from above downwards in the upper half of the iris and from side to side in its lower half.

The lens appears highly curved and extremely translucent. The shagreen is easily visible but no sutures could be made out. The vitreous could not be seen.

Ophthalmoscopic examination.—The fundus reflex was a pale, silvery green. The details of the fundus were very easily seen with an electric ophthalmoscope, the refraction being hypermetropic.

The optic disc was situated below and to the nasal side of the posterior pole. It was a slightly kidney-shaped oval, its long axis vertical and its concavity towards the temporal side. It was white in colour, with some greyish areas in the centre and round the edges. In the centre were a very few red capillaries, arranged in small loops, and not extending to the edge of the disc. There is no pecten.

The nerve fibres can be easily seen radiating from the disc. They have a silky sheen, most marked near the disc, and becoming gradually less visible as they pass to the periphery. They are non-medullated, and are much more easily seen than are those of mammals, possibly because of the greenish background. Their arrangement is interesting, being almost exactly similar to that found in man. On the nasal side of the fundus they radiate evenly from the disc, while on the temporal side they sweep round in a curve above and below the posterior pole, leaving a very definite *area centralis* in the situation of the human macula, and meeting in the beginnings of a temporal raphé outside this. The *area centralis*, although the macula itself could not definitely be seen, shows modification from the rest of the fundus, being dark in colour, and more stippled. The general fundus colour is a speckled greyish green, shading into a browner tint at the posterior pole. The whole retina is covered with minute reflecting dots, almost exactly like Crick's dots, and probably caused by the same structures (Müllerian foot-plates). There are no vessels in the retina, and the choroid is not visible through it.

This brief demonstration may be of interest in showing firstly, how extremely early one can find evidence of specialization of the posterior pole for form vision,

and secondly, how such an animal as sphenodon maintains its reputation as a "generalized reptile." As examples of this, one can cite (*a*) the vertical pupil (as in crocodiles and geckos); (*b*) the vascular pattern of the iris (intermediate between crocodiles and lizards); and (*c*) the absence of a pecten, the presence of capillaries on the optic disc only (resembling the fundi of some primitive marsupials), and the specialization of the posterior pole (a character found even in some invertebrate eyes).

Sir JOHN PARSONS said that in her excellent communication Miss Mann had omitted to mention the most striking feature of sphenodon, namely, the fact that it possessed a pineal eye: it had a definite persistent eye corresponding with the position of the pineal gland. Professor Dendy and Professor Baldwin Spencer had described this eye many years ago.

What Miss Mann said about the macula was very interesting; he (the speaker) had searched the literature to find out more about the macula. When reading about the comparative anatomy of the retina in the books available, one found vague remarks about the "area centralis," etc., which were difficult to correlate. He agreed that further research into the structure of the retina, from that standpoint, was badly needed. The difficulty was chiefly that of histological examination of rods and cones.

He had now reached a stage of great diffidence in describing the neuro-epithelium of any lower animal as a "rod" or a "cone"; he considered it was better to eliminate those terms. In human anatomy rods and cones had a definite meaning, though, even there the most typical cone was of rod-like structure. But it was so mixed up with the duplicity theory that it was better to keep free of the terms "rods" and "cones."

Another point of great interest was the development of a more highly differentiated retina than was ordinarily described—the area centralis—more like true macula. That this should be found in so lowly a species as sphenodon was very important.

With regard to maculæ in birds and Sauropsidæ and in primates, these were developed along different lines, and in different environments, and this fact had to be borne in mind when allocating them as "earlier" or "later" in the phylogenetic scale. In sphenodon there was probably a very primitive condition, which had later diverged into various types, with the result that there was a macula in the bird which was like the macula of the primate or the human being morphologically, but not to be regarded as the same thing. The two things developed and diverged, and specialized in their own particular way.

That was only part of what he felt strongly as to the correlation of human sensations and the psychology of perception, etc., with results which were derived from observations on lower animals of different species. It was doubtful whether one could take these things in one species and transfer them to another. The question of the macula now raised was an example of the necessity for care in that respect.

Sarcoma of the Choroid: Further Report on Case Previously Shown.—HUMPHREY NEAME, F.R.C.S.

The patient (Mrs. B. P.), aged 50, was shown at the meeting of November 13, 1931. A history was given of micropsia and slight disturbance of the central colour vision, noticed by the patient two years before. There was some evidence of the development of hypermetropic astigmatism in place of myopia and myopic astigmatism in the left eye. The left fundus oculi showed an oval swelling in the macular area projecting into the vitreous (see fig. 1).

Fuller details of the case are recorded in the *Proceedings*, 1932, xxv, 473, Sect. Ophth. 15.

The left eye was enucleated in November, 1931.

Pathological examination. (Royal London Ophthalmic Hospital Path. 206/1931).—The eye was fixed in 4% formaldehyde. It was divided horizontally above and below its centre. Macroscopically a pale ovoid mass projected forwards in the macular area causing a somewhat gradual detachment of the retina all round. Slight pigmentation was seen on its lower surface. The mass was 6 mm. in its horizontal diameter and 5 mm. vertically.

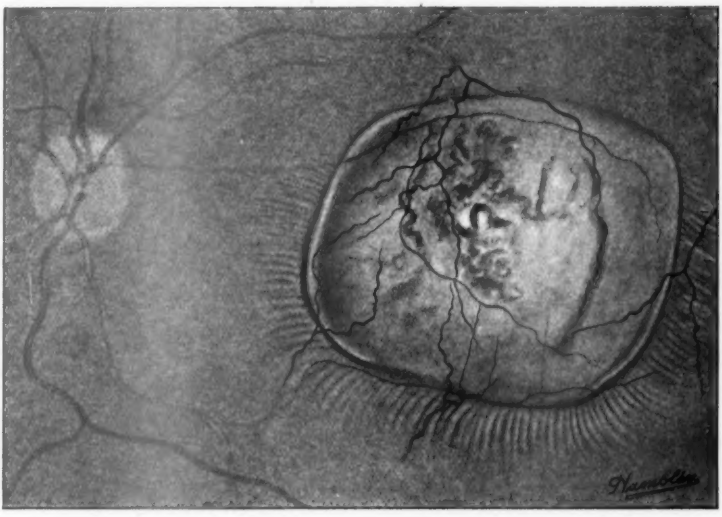

FIG. 1.—FUNDUS DRAWING OF SARCOMA OF CHOROID IN MACULAR AREA OF THE LEFT EYE.

The features which enabled a diagnosis of malignant growth to be made were (1) the apparent solidity and fixity of the mass as seen with the ophthalmoscope; (2) the presence of some pigment on the inferior part of its visible surface; (3) the numerous vessels all over its surface deep to the retinal vessels; and (4) the numerous delicate retinal folds at various places at and beyond its margin, indicating traction on the retina and precluding a diagnosis of retinal cyst. The age of the patient lent further support to the conclusion that a malignant growth was present.

(Microphotographs by Mr. Macdonald of the Photographic Department, University College Hospital Medical School.)

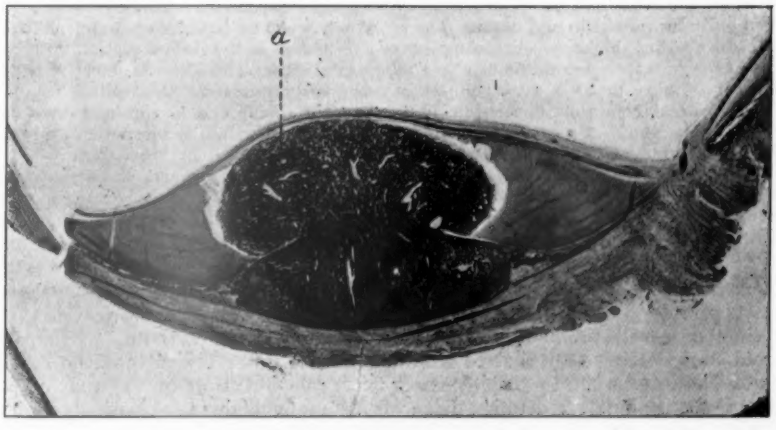

FIG. 2.—SARCOMA OF CHOROID.

Microphotograph of horizontal section (× 7·5 diam.) of the growth (in the macular area) and the posterior part of the eyeball. The optic nerve is near the right-hand of the section. A typical mushroom-shaped growth is seen arising from the choroid; "*a*" identifies the portion shown in fig. 3.

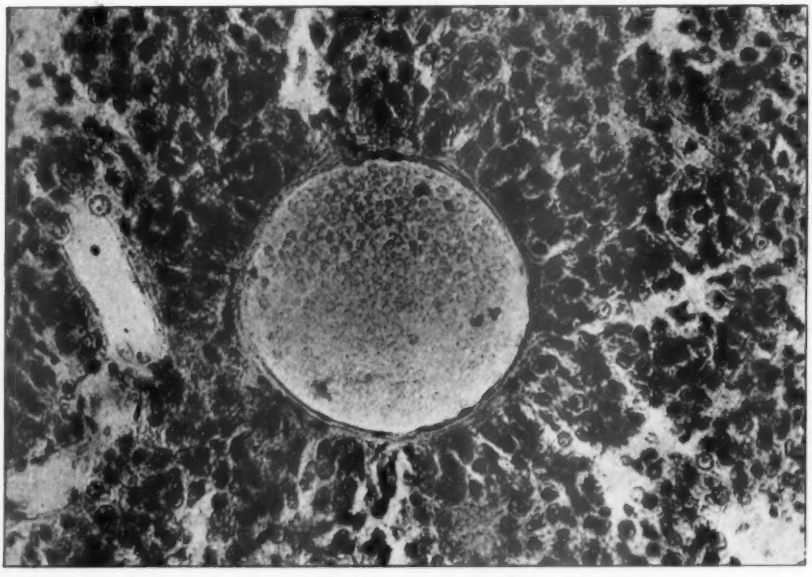

FIG. 3.—SARCOMA OF CHOROID.

Microphotograph of part of the more recent mushroom head (*a* fig. 2, × 350 diam.). The size of the different structures can be recognized by comparison with the red and white corpuscles in the blood-vessel. The growth cells are large oval cells with circular or oval nuclei and with a darkly-stained nucleolus in each.

Microscopic examination.—The central portion was embedded in celloidin. Sections were stained with hæmatoxylin and eosin. The growth is seen to be of mushroom shape (see fig. 2). Its greatest thickness—antero-posterior—measured in the stained section through the centre of the growth is 4·5 millimetres. Under examination with Zeiss A objective with No. 4 E.P., it is seen to be a very cellular growth, with numerous thin-walled capillaries, especially vascular in the mushroom head. Bruch's membrane is ruptured and curled forwards at its edge. No connective tissue stroma is seen within the growth. Only a few slightly pigmented cells are discovered on careful examination.

Under Zeiss D objective and No. 4 E.P. (fig. 3), the growth is seen to be composed of oval cells with oval or circular nuclei each containing a small darkly-stained nucleolus. The numerous capillaries possess walls formed of a layer of endothelial cells.

The growth has the appearance of a spindle-celled sarcoma of the choroid.

Conclusions.—The history of slight disturbance of colour vision in the left eye suggests strongly that the commencement of malignancy dates from two years before the time of enucleation. It may be presumed that a pre-existing nævus of the choroid started about that time to extend from the outer layers into the capillary layer and so to interfere to a slight extent with the nutrition of the rod and cone layer of the retina. A definite diagnosis of malignancy was justifiable on the following grounds: (1) the solid and fixed appearance of the growth; (2) the pigmentation, slight but quite distinguishable, on the lower part of the visible surface; (3) the presence of numerous vessels on its surface beneath the retinal vessels; (4) the delicate retinal folds arranged in a more or less radiating manner

from the margin of the growth for a considerable part of its circumference. It had been suggested that the mass should be punctured with a needle passed through the sclerotic laterally and through the vitreous to enter it on its visible surface while under ophthalmoscopic examination. The result of this procedure—in any case difficult to carry out—is open to a false interpretation. The writer reported in the *Transactions of the Ophthalmological Society* in 1920[1] a case of cyst of the retina in a man aged 27, in which a diagnosis of choroid sarcoma had been made. In the latter case the mass was considerably towards the periphery of the fundus and transillumination gave a dark shadow. The explanation of this positive result was that the cyst contained blood, as was discovered on histological examination. In such a case of a blood-containing cyst, the introduction of a needle would quickly flood the vitreous with blood and suggest that a vascular neoplasm had been penetrated. The coincidence of a retinal cyst with a blood-content must, however, be so extremely rare that the procedure of puncturing the mass is worthy of adoption in a really doubtful case. The retinal folds presumably indicate rapidity of growth of the neoplasm. The main bulk of a retinal cyst lies external to the general level or plane of the detached retina immediately adjacent to it. That is to say, the cyst bulges more externally than towards the vitreous. The least rare cyst occurring in the internuclear layer is here considered. A cyst therefore might be expected to exert as great a strain on the surrounding retina as a choroid neoplasm pushing the retina in front of it. Such a cyst, however, is probably of very slow development, and less likely therefore to produce rucking or folding of the retina. In view of the rarity of rucking of the retina in cases of choroid neoplasms, it is probable that the sarcoma in the case described had in the last few months grown with unusual rapidity. The prognosis is therefore in all probability more serious.

(Acknowledgments are due to Mr. Stallard, Curator of the Royal London Ophthalmic Hospital, for having the sections prepared.)

Discussion.—Mr. A. HUGH THOMPSON said he was not present when this patient was shown in November, but he saw her on March 25, when she was under the care of Mr. Holthouse. At that time there was no suspicion of a new growth; the fundus appeared to be normal. The vision had been deteriorating for a year. The pupils were equal and reacted, and the discs were normal. The vision of the right eye was normal, with low myopic correction, the left eye had $\frac{6}{18}$ with correction of + 2·0 D., but there was a distinct paracentral scotoma down and in from the fixation point about 30°. The condition was then thought to be some form of retro-ocular neuritis, and subsequently the patient was admitted to hospital.

Sir JOHN PARSONS said that Mr. Neame had not laid sufficient stress on the presence of an entirely different system of vessels beneath the retinal vessels. He had himself regarded that as the only clinical absolutely pathognomonic sign of new growth. He did not think the question of a cyst arose if there was a different set of vessels clearly visible, as in this case, and obviously unconnected with the retinal system. He asked whether there was a simple detachment in the lower part of the fundus at any stage in the case. He, the speaker, had pointed out that however small the sarcoma might be, there was frequently a simple detachment in the lower part of the fundus; that the growth seemed to act as an irritant of the choroid, as that fluid gravitated to the lower part of the globe, and a simple detachment occurred there. In his "Pathology" there was an account of a case of a small sarcoma exactly in the macular region. The case was under the care of Mr. Marcus Gunn. There was a slight swelling and a small growth. The field of vision showed no loss over the spot where it was expected, but there was a definite gap in the field corresponding to the detachment which was then discovered in the lower part of the fundus.

[1] Neame, *Trans. Ophth. Soc.*, 1920, xl, p. 161.

Mr. HUMPHREY NEAME (in reply) reminded Sir John Parsons that in his paper he included the vessels as a point of importance, and the presence of pigment, the solidity of the growth, and the retinal foldings around it, as signs which justified the diagnosis of malignancy. The fields, as taken by the house surgeon, showed no abnormality apart from a large scotoma.

He had been surprised at his patient's history of two years, with rapid growth during two months. She was seen in March, and nothing was then to be made out. Probably the condition in the eye then was one of non-pigmented mole or nævus of the choroid. When no pigment was present in such a mole, presumably one could not recognize its nature.

Section of Laryngology.

President—Mr. WALTER G. HOWARTH, F.R.C.S.

[*February 5*, 1932.]

DISCUSSION ON THE COMMON COLDS AND THEIR SEQUELÆ.

StClair Thomson: Wisdom comes, but the Common Cold not only lingers but remains elusive.

The sterile nose.—Possibly I have been honoured with the invitation to open this discussion as it might be thought that I should by this time know something about it, since it is twenty-one years since I committed to a textbook my views on the Common Cold.

The researches recorded therein, carried out in collaboration with Professor R. T. Hewlett thirty-seven years ago, have stood the test of time.

We were able to demonstrate that the nose, in normal conditions, contrary to what had previously been taught, filters off all dust and micro-organisms from the air before they can reach the larynx, dealing possibly with as many as 14,000 organisms during one hour's tranquil respiration. This successful defence of the lower airways was found to be largely due to the ciliated epithelium which is able to move a fragment of cork along at the rate of 25 mm. (1 in.) a minute. An interesting confirmation of a similar rate of eviction from the sinuses was recorded thirty years later by Lowndes Yates. On injecting 10 c.c. of an indigo-carmine solution into the antrum, the coloured solution, if the sinus was normal, appeared in the naso-pharynx in about two minutes.

But in spite of the cilia, the inhibitory mucus, and other protective arrangements, the defence put up by the nose against infection is sometimes overborne and we contract a Common Cold. The view that this affection was infectious was advanced in my textbook at a time when it was far from being generally recognized. It is not yet universally accepted; and I find I must to-day repeat much of the evidence collected twenty-one years ago.

Beyond adding fresh evidence that the Common Cold is an infectious disease, I fear that medicine can claim but little progress as regards the ætiology, prevention or cure of this, the most common of all the "sufferings of this sin-sick earth." We might, comparing the "Cold" with other diseases, apostrophize it as Matthew Arnold did Shakespeare in referring to his elusive personality:—

> "Others abide our question. Thou art free.
> We ask and ask. Thou smilest and art still,
> Out-topping knowledge."

Definition.—Some of the literature on the subject is diminished in value as observers have confused together a study of influenza, primary pharyngitis, laryngitis or bronchitis, spasmodic rhinitis, asthma, or primary sinusitis. My effort at a definition of our subject is as follows: The Common Cold is an acute or subacute catarrhal affection, commencing in the nose or postnasal space, generally invading

the sinuses and sometimes spreading to the Eustachian tubes, the pharynx, the larynx, or further. It may leave a chronic condition, locally or elsewhere.

Frequency.—It is hardly necessary to emphasize the frequency of the Cold, otherwise it would not be generally known as the "Common" Cold.

In six public elementary schools in Sheffield 30% of absences were due to Colds (J. A. Glover). Colds and "feverish catarrh" (excluding influenza) account for 25% of the admissions to a public school sanatorium (Lemprière).

At Rugby School in the three terms of 1920 there were respectively 64, 260 and 56 cases, and in the three terms of 1921 the cases numbered 243, 42, and 21. It was calculated by Dr. A. I. Simey that, on the low estimate of ten days for each case, in these two years seven thousand school days (or about twenty years of school life) were lost.[1]

Season.—As to the period of the year when the Common Cold is most prevalent the investigations of the U.S. Public Health Service tend to show that the greatest frequency is in the latter part of January (153·3 per 1,000); this declines until the latter half of June, to increase sharply at the end of July and beginning of August up to a peak (120 per 1,000) at the latter half of September. Then comes a decline until a sharp rise (126 per 1,000) in the latter half of November. From this date there is a decline (65) till the end of the year.

Pre-disposition.—It is generally recognized that Colds are least common at the two extremes of life—infancy and old-age. Incidence is most frequent during the first four years of life, next between the ages of five and nine, and generally diminishes with advancing years (Warren Sisson).

An interesting investigation of large groups of students in Cornell University showed that in 815 freshmen 60% had colds two or three times a year, 15% never more than once a year, and 25% four or more times a year. Taking the two extreme groups (the one-or-less-a-year group and the four-or-more-a-year group) there was no marked difference between the two as regards: Smoking, history of operation on nose or throat, exposure to irritant dust or gas, mouth breathing, sleep, exercise, draughts, wearing of flannel next the skin, goloshes, daily cold bath, tendency to perspiration, chronic constipation, or family history.

A further study as regards the cold-susceptible group and what we might call the "normal" group, in regard to past history of infectious disease, suggested the two following conclusions:—

(1) The general physique and the physical defects in cold-susceptible College students are much the same as in normal students.

(2) Cold-susceptible College students present a history of more infectious disease, asthma and hay-fever than do normal students (4·31 infections per person, compared with 3·38).

Ætiology.—In an endeavour to co-ordinate our views, and the knowledge we at present possess, I propose to consider the possible factors of causation as follows:—

A. (1) Atmospheric causes, chiefly a low temperature. (2) Cold as only a predisposing cause.

B. Disturbance of metabolism.

C. Infection.

Cold (*Low atmospheric temperature*).—As might be expected, France—the country of the dreaded "courant d'air"—is the most devoted supporter of the age-old opinion that a Cold, as its name applies, is due to cold. A personal friend of mine has written an excellent and much-quoted "Essai sur le rhume simple ou coryza." But he still holds that of all predisposing influences the most important is cold, particularly if moist and prolonged. He considers this to be the cause of the loss of tonus of the vasomotor system of the nose.

1 *Journ. Roy. San. Inst.*, 1927, xlvii, 475.

Now here it is assumed that a Cold is due to chilling because it is most frequent in the coldest months. But there might be several other explanations of this coincidence, the most evident being that during cold weather people spend more time in vitiated air, in closer proximity, so that infectivity is favoured. Indeed, Leonard Hill and F. F. Muecke have shown that nasal turgescence and congestion are produced by a warm, ill-ventilated atmosphere and that this tendency is increased by exposure to a lower temperature. In other words, it is the warm, stagnant, vitiated atmosphere which originates the catarrh.

Very full investigations have been carried out in Johns Hopkins University on "Upper respiratory disease (Common cold) and weather." The general conclusion of the report is as follows:—

"The evidence presented in this paper strongly suggests that changes in weather during a warm season are probably more associated with upper respiratory disease (Common Cold) incidence than changes in weather during a cold season."

Recently I discussed the subject with a member of a Greenland expedition. He confirmed the experience of all Arctic and Antarctic travellers. Mr. Courtauld, who had lived for some months under the snow without a cold, promptly contracted one as soon as he got on board the ship to take him back to Denmark.

Per contra, as we might say, the Metropolitan Life Insurance Company of New York records that in winter the indoor, sedentary worker has four times as many Colds as soldiers, and nine times as many as taxi-drivers!

Metabolism as a cause.—Some would regard Colds as merely an expression of a special type of disordered metabolism—as instanced in the "carbohydrate child" or the "protein child" in whom faulty dieting is accompanied by an undoubted susceptibility to catarrh. Indeed, V. S. Cheney, of Chicago, boldly states that Common Colds are not infectious. He considers a Cold as a local manifestation of a systemic disturbance—a "mild acidosis." He bases this conclusion on (i) the reproduction of all the symptoms of a Cold by inducing an artificial acidosis by the administration of ammonium and calcium chloride; (ii) the degree of severity of the Cold symptoms being in direct ratio to the degree of acidosis induced; (iii) the successful results of the treatment of Colds by thorough alkalinization; and (iv) his failure to reproduce a Cold in healthy persons by inoculating them with the secretions of an individual suffering from an acute Cold. He suggests that the seeming contagiousness is due to similar unhygienic conditions in a group of individuals.

He regards the infectious origin of a Cold as only an unproved theory, because in early stages the secretion is sterile and the organisms often regarded as factors are only secondary invaders of the later stages.

A filterable virus.—An extensive and very important work on the possibility of a filterable virus being the cause of a Common Cold has been carried out by Dochez and co-workers in New York.

Treatment.—The first principles are early diagnosis and early treatment. If every individual at the first threatening of a Common Cold went to bed and remained there for from thirty-six hours to three days, in an isolated and well-ventilated room, he would not only cease to be a focus of infection but he would curtail his attack and escape most, if not all, complications. Every case of established chronic sinusitis—with, perhaps, the few exceptions of those originating from a tooth, from a septic swimming-bath, or some similar cause—started as an acute sinusitis, generally part of a common cold. I have never had to treat an early acute sinusitis which did not completely resolve if treated with bed rest, warmth and other methods to be touched on presently. I have never seen a fatal complication in an acute sinusitis so treated.

In addition to isolation and rest in bed, I need only mention warmth to the

head (radiant heat, von Eicken's heat box), avoidance of nose lotions and sprays, the use of steam inhalations of menthol, eucalyptus, benzoic acid. The use of suction is of doubtful value. Drugs should only be used to relieve symptoms, and the comfort of salicin, the salicylates, aspirin, phenacetine is common knowledge. When the mucous discharge becomes muco-purulent it generally means the invasion of the sinuses. If a purulent invasion of one or both maxillary sinuses is diagnosed simple saline lavage should be employed.

John Freeman: Throughout its history both the laity and the profession have held that the cold is infectious. On this point the "steamer colds" of the Scotch Islands present a crucial experiment if confirmation were needed. In pre-bacterial days living germs were not imagined in infections, but when bacteriology came in, bacteria were sought and found in the common cold. In the mouths of all of us at all times are a number of diverse microbes, but after the onset of the cold one or more of these types is enormously increased in numbers, and to such an extent as to be obviously an infection. The micro-organisms which cause the bacterial infection in the cold are pneumococci, streptococci, Pfeiffer's bacilli, diphtheroids, micrococci of the catarrhalis type, Friedländer's bacilli and other coliforms, and staphylococci. Those who examine such cases find that there are little overlapping epidemics sweeping through the population during the catarrhal season; for a week or two we may perhaps find only the pneumococcus, then possibly Pfeiffer, then a streptococcus maybe. I must emphasize that there is no doubt of these infections that they cause the bulk of the symptoms of a bad cold, and are responsible for nearly all the danger in sinusitis, laryngitis, and bronchitis.

For many years it has been noted that the watery discharge which ushers in some colds is almost bacteria free, and attempts have been made to explain this or to find an undiscovered germ; to-day the idea of the filterable ultra-microscopic virus holds the field. In 1914 Kruse filtered the discharge, proved that the filtrate was bacterially sterile, and with it transmitted typical colds to two-fifths of the healthy men on whom he tested it. Since then this work has been contradicted, repeated, or explained away, but now seems proved by Dochez and his fellow workers in New York; both to man and to the chimpanzee, and through a series of men or chimpanzees will this bacteria-free filtrate transmit colds. From the time of instillation to the onset of symptoms there is an incubation period of from three to four days; after such an attack there is protection for three months (at any rate in the chimpanzee); because this protection does not cover against influenza Dochez deduces that the influenzal virus must be different from that of the cold. He asserts he has grown his virus, still invisible and still filterable, on a succession of thick embryo tissue cultures and after that could produce a typical cold with it; it is destroyed by heat as is a microbe or a ferment; lastly, and significantly, the virus causes increased growth of the bacteria which we have noted as infecting in the second stage of the common cold.

If we take it as proved that a virus initiates colds, we do not know if it initiates all colds or how many viruses there may be; if it can act alone or what co-operating factors there must be; we do not know if it is alive or is a complex chemical agent like a ferment; we do not know yet how to prevent its action or to cure it when it comes. We might be able to extirpate it as we have extirpated rabies, but at present we have not enough knowledge. Meantime the trouble from the virus itself seems to be trivial, but from the bacterial infections which it induces we have both trouble and danger.

Until we have found the specifically bacteriotropic antiseptic, any chemical which can combine with and so kill bacteria must also damage our living

tissues; if it is too weak for that, or if we use hypertonic salt solution for douching or gargling we wash away the natural protection of the lysozymes and so again do more harm than good. But all these devices probably afford psychological support to the sufferer, and with regard to the psychological factor, Dochez in his very human and readable account, says that his volunteers were sometimes too volunteering and would produce a cold because they thought the experiment needed one—a complication he escaped when dealing with chimpanzees.

The bacterial factor in colds can be dealt with either by reducing the chances of infection or by protecting against it with a bacterial vaccine. A vaccine is eminently suited to treating small localized infections, but we must give bigger doses to achieve prophylaxis. If we use such a dose in the catarrhal season we risk bringing on an infection with a run, and patients then complain that they are made worse; therefore the requisite dose must either be given in the non-catarrhal season or attained step by step. However reached, maintaining doses should be given every month as the immunity is short-lived.

Dan McKenzie wished to say a few words on treatment. It could be looked at from the epidemiological—that is, the preventive—point of view, but knowledge was so vague that there was no method by which it could be controlled on the principles of epidemiological science. The key to the position he considered to be the carrier. Many people were carriers of the infection of the common cold without having any nasal sinus trouble, and in them no disease of the nose was present between the acute attacks. Yet at least twice a year these people had acute colds in the head, with the accompanying symptoms and sequelæ. It could therefore be assumed that they were harbouring the causal virus during the latent periods. The reaction of the system during the acute attack produced a degree of immunity, but only of limited duration. During their acute illness carriers seemed to become infectious to their neighbours.

CASES.

Epithelioma of Pharynx treated by Diathermy.—DAN MCKENZIE.

A man, aged 60, was operated on by diathermy in Johannesburg in February, 1930, and again in February, 1931. The neck was not cleared, but X-rays were applied externally in August, 1930, and again a few weeks ago. The neck presents the unusual appearance, for pharyngeal carcinoma, of infiltration of the skin *en cuirasse*, as a result of which, with lymphatic obstruction, the laryngeal mucosa has become œdematous. But there is no sign of any recurrence of the disease in the pharynx. The case illustrates an effect of diathermy removal to which I have already drawn attention; namely, the influence of the abolition of sepsis in retarding the progress of the disease and rendering it more endurable. A drawback to the insertion of radium into an epithelioma of the pharynx is the introduction or dissemination of septic infection.

Endothelioma of Naso-pharynx treated by Radium.—J. F. O'MALLEY.

J. D., male, aged 65, on October 8, 1930, came to University College Hospital complaining of nasal obstruction, especially on the right side, for three months, and of deafness in the right ear for one month. A hard smooth mass could be felt in the naso-pharynx, its lower border being visible below the uvula. Several small lymphatic glands were felt in the anterior and posterior triangles of the neck and in the left axilla.

On October 27, 1930, a portion of the growth was removed for microscopic examination and six 2-mgm. radium needles were inserted. All the needles worked loose at intervals, during the next three days, so that the total dose amounted to

500 mgm. hours. The mass continued to diminish in size for six weeks, which enabled the patient to breathe through the nose and hear normally with the right ear. As there was some growth visible still to a post-nasal mirror examination, on December 8, 1930, four 2-mgm. needles were inserted. Two of these became loose within twenty-four hours and two remained for seven days, the dosage being 690 mgm. hours, which together with 500 mgm. previously gives 1,190 total dosage. On December 18 the patient received 500 R. units of deep X-ray therapy on the right side of the neck and a similar dose to the left side on the 20th. He has remained free from any symptoms or signs of the growth for over a year.

Acute Pansinusitis with Proptosis of Eye. Recovery without Operation.—E. R. G. PASSE (introduced by HAROLD KISCH).

Patient, a man, aged 41, on December 13, 1931 awoke with left frontal headache and vomited on rising. The next day the headache increased and a discharge commenced from the left nostril. On December 15, there was spasmodic pain over the left eye. Patient vomited several times; vision of left eye became blurred. Felt too ill to work. Eye slightly bulged.

Examination showed slight œdema of left eyelids, proptosis of left eye downwards and outwards. Limitation of all movements, especially of internal rotation. Retinal veins dilated. Maximum tenderness in floor of frontal sinus. Nose contained pus coming from left ethmoid region. Left maxillary antrum contained pus. X-ray showed frontal, ethmoid and maxillary sinuses opaque.

Under local treatment and repeated antral lavage the condition subsided, the pain subsided first, and the œdema and proptosis disappeared towards the tenth day.

January 15, 1932.—Vision and movements normal. Discharge slight.

United Services Section.

President—Lt.-Col. E. M. Cowell, D.S.O., R.A.M.C. (T.A.).

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Some Medical Problems of Mustard Gas Poisoning.[1]

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(late R.A.M.C.).

In the European War the introduction of weapons which distributed asphyxiating, poisonous, or other gases, and analogous liquids and materials, added to the heavy responsibility which the Medical Services already carried, and presented them, and the research laboratories which served them, with new and intricate problems. In the later stages of the war the development of chemical warfare necessitated the creation of a special organization, from which the Chemical Defence Research Department has evolved. All the early anti-gas work was done under the ægis of the Army Medical Department, and much of it in this College. The names of Colonel Sir William Horrocks and Colonel P. S. Lelean stand out as those of pioneers in the organization of anti-gas research.

Before the German gas attacks in April, 1915, little was known outside the laboratory of the pathological action of many of the substances used in chemical weapons. It is therefore not remarkable that there was, at first, some confusion of thought as to the manner in which lesions were produced, and that lines of treatment should have been followed which, on a clearer understanding, were dropped.

The lack of knowledge of the action of chemical warfare materials, and the terror which they inspired created a false impression of their deadliness, which was fostered by propaganda. However, a study of the invalidity figures of this and other countries, particularly those in the last volume of the Official Medical History of the War, makes it clear that against a disciplined force properly equipped with anti-gas appliances, and trained to use them, chemical weapons caused no more destruction than other weapons of war. Nor is there anything to show that the suffering they caused was greater than that inflicted by other weapons.

Research carried out during and since the war has enabled us to classify these poison gases according to their physiological action. The methods of studying them have been standardized, and it is now possible rapidly to assess the potency of a particular substance and the type of lesion it will produce. Incidentally, this work has given, and is giving, considerable help in the problems of protection of workers in hazardous industries.

We now divide warfare gases into three broad classes: (1) Tear gases, or lachrymators; (2) lung irritants, including the true lung irritants, e.g., chlorine and phosgene, and the irritant smokes which are mostly solid organic arsenical compounds; (3) the vesicants.

Much has been said regarding more deadly gases which may be used in future wars, but although over a thousand compounds have been examined in this and other countries, so far as I am aware no substance has been found which is of a wholly greater order of potency than those already used. It is, however, clear that the known warfare gases could be used more effectively than they were in the European War.

I shall chiefly consider the vesicant—mustard gas—the most potent of all the chemical weapons as a producer of casualties. However, our respirators now give complete protection against any concentration of the warfare gases likely to be met with in the field. Amongst other nations also, respirator research has developed

[1] We regret to record the death of Major Galwey which occurred while this paper was passing through press.—[Ed.].

greatly, and it is thought that most nations now have adequate protection in this respect.

Like all other chemical warfare agents, mustard gas was discovered in the course of ordinary research long before the war. Its chemical name is dichlorodiethyl sulphide. In its pure state it is a clear, colourless and somewhat oily fluid, with only a faint odour. It boils at 217° C. (412° F.), and becomes a white crystalline solid at 14·4° C. (58° F.). It is heavier than water, it vapourizes slowly at ordinary temperatures, and so tends to persist on the surface on which it falls.

Since pure mustard gas freezes at a relatively high temperature, it is used in chemical weapons mixed with a suitable solvent. As generally used it is a dark heavy liquid, which leaves a stain, and whose odour is more pronounced that that of the pure compound. It freezes at about 7° C. (44° F.).

Mustard gas has certain outstanding features which must be remembered:—

(1) *Stability.*—It is not easily broken down into harmless compounds by substances ordinarily available in the field.

(2) *Solubility.*—Whether as vapour or as liquid, it is readily soluble in many oils, such as fuel oils and greases, animal and vegetable oils and fats, and in organic solvents, such as petrol, alcohol, chloroform, etc.

It is slightly soluble in water (under 1%), but the solution is dangerous to handle. On solution it is gradually hydrolysed to a harmless compound.

(3) *Persistence and powers of penetration.*—Like an oil it penetrates most ordinary substances, but does so more readily. Once it has penetrated, being persistent, it will give off toxic vapours for a time depending upon the prevailing weather conditions. The vapour of mustard gas readily penetrates all ordinary clothing.

(4) *Odour.*—Since at present the most sensitive means of detecting mustard gas in the field is by the human nose, it is important to be able to recognize its characteristic odour. It has been likened to mustard, to horse radish, onions and garlic. It is important to remember that, as with other odours, the sense of smell becomes quickly fatigued, so that after a time in a mustard atmosphere one fails to recognize it. On breathing pure air for a short time, as for instance by wearing a respirator, the sense of smell recovers.

(5) *Toxicity.*—Both as vapour and as liquid, mustard is exceedingly poisonous. A drop 1 mm. in diameter will produce a blister the size of a sixpence. But it is essentially a local poison, acting only on those tissues with which it comes in contact. The eyes are the organs most sensitive to mustard gas, next the lungs and respiratory passages, and last the skin.

(6) *Insidious action.*—Small drops of mustard falling on the skin do not attract attention by a sensation of cold as do more readily volatile substances, nor do they at once cause smarting or other sensations, so that contamination may be unsuspected.

(7) *Delayed action.*—There is always a delay before the onset of the signs and symptoms. This period depends upon the concentration of the gas and the length of exposure. The action is cumulative, so that prolonged exposure to low concentrations may result in injury.

It is important to note that although we speak of a delayed action in mustard gas poisoning, this delay is only clinical, i.e., no gross signs or symptoms are manifest until some hours after exposure. In reality, damage to tissue begins immediately mustard gas has penetrated the cells, and as early as ten minutes after its application to the skin of a rabbit, microscopic examination gives evidence of damage in pyknotic nuclei, shrunken cells, dilated blood-vessels and commencement of leakage from the blood-vessels.

(8) *Delayed healing.*—Mustard gas penetrates the skin rapidly, and once it has penetrated deeply there is marked delay in healing of the resulting lesion. The tissues are devitalized, and as a result are readily abraded by rubbing or pressure, and form an excellent nidus in which organisms flourish. On the other hand, if the

injury is only a mild inflammation or superficial blisters, the condition may clear up in a few days.

(9) *Sensitivity.*—Some persons are hypersensitive to mustard gas. It is not yet certain what proportion of an average population such hypersensitives would form; it would probably be very small. Hypersensitivity can be acquired, and some research workers, after a series of mild burns incurred during experiments, have become so sensitive that if only minute traces of mustard gas are present they react fairly severely. It may be that amongst troops repeatedly exposed to mustard gas such acquired hypersensitivity would become a serious matter.

Mode of action.—In spite of prolonged and exhaustive research, we are still ignorant of the mode of action of mustard gas. We know by microscopic examination of sections of skin and other organs the sequence of events following its application, but we know little or nothing of the underlying mechanism by which these events are brought about.

Some fourteen hypotheses have been advanced to explain the action of this substance, but in every case either experimental observation has disproved it, or experimental confirmation is lacking. I shall, however, outline the more important of these to illustrate the complexity of the subject. The earliest is :—

The acid hypothesis.—Mustard gas on hydrolysis breaks up into hydrochloric acid and thiodiglycol, and it is believed by the supporters of this theory, amongst whom are Marshall and his co-workers in America [1], that this liberation of acid causes the damage in the tissues.

Peters and Walker [2], however, in this country have shown that the rate of liberation of acid in a series of allied compounds does not run parallel with their vesicant action. Many substances which liberate acid are non-vesicant, and vice versa. They further point out that the cell, by means of its buffering system, is well able to cope with small quantities of acid. Application of alkalies to a mustard burn aggravates rather than alleviates it.

The sulphydryl hypothesis.—This was developed as the result of investigating the possible interference of toxic agents in oxidation-reduction processes. It postulates that irritant action is the result of destroying the sulphydryl constituent of tissue. There is no evidence that mustard gas itself affects the sulphydryl group, but mustard gas on oxidation forms a sulphone, and although *in vivo* no evidence has been obtained of the sulphone affecting the SH group, *in vitro* it was found that sulphone did inhibit oxidation involving this group.

The sulphone of mustard gas has been shown to be on injection more toxic than mustard gas itself. We have, however, been unable to obtain any evidence of the presence of sulphone in the tissues after the application of mustard gas.

Lewis [3] thinks that mustard gas acts by the liberation from the cells of a histamine-like body. This may be so, but it does not explain how mustard gas initiates the production of such a substance.

Stimulation of sensory nerves.—Dixon [4] claimed that mustard gas acts by stimulating sensory nerve endings, which initiates an axon reflex with resulting dilatation and leaking of capillaries. It has, however, been found that mustard gas is quite effective on denervated skin.

It will be seen from this brief summary that none of the hypotheses so far put forward has given a satisfactory explanation of the action of mustard gas, nor has it been found possible to determine whether the sulphur atom or the chlorine atom is responsible for its toxicity. The clinical picture of mustard gas poisoning is well known from official text-books.

After this brief survey of its characteristics we will turn to the problems which will confront us should mustard gas be used in another war.

We must first consider the ways in which it was used in the last war, and compare their effectiveness with those in which it might be used in future. The only weapon used to distribute it during the war was the artillery shell. In some cases the shell was fitted with a burster just sufficient to open it and disperse the liquid, causing gross contamination of the object on which it fell—a contamination likely to persist for a considerable time. In other cases the burster was more powerful, distributing the mustard in fine drops, whereby the immediate danger from vapour was increased, and the persistence lessened. That these methods were effective, witness the number of casualties produced. It is thought, however, that under the conditions of static warfare these casualties were caused by men carrying contaminated soil on their clothing or boots into dugouts and billets, and that the mustard gas vapourizing from such contaminated clothing gassed the wearers and their companions. It is probable, too, that a large number of casualties were due rather to exposure to vapour than to contact with liquid.

But mustard gas can be so distributed as to expose troops to greater danger, either by contamination by liquid drops or by much heavier local concentrations of vapour. I refer to distribution from aircraft. Aircraft were never used for the discharge of gas bombs during the European War, but it is said that the Spaniards discharged mustard gas bombs in their war against the Riffs. Mustard gas can also be sprayed from the air in much the same way as smoke curtains are laid, or crops sprayed with insecticides; it will come down from great heights, and drops will travel in an effective form with the wind, so that troops in the open could be sprayed by an aeroplane several miles away and at a great height above them. During a retreat or in defensive operations mustard gas can be distributed by watering carts or watering cans.

Therefore in a future war, if gas is used, troops may be subjected to more severe contamination than hitherto, with consequently severer injuries necessitating more prolonged treatment. Further, this weapon, if used from the air, may affect not only troops in the fighting line, but also those on the lines of communication and at bases; hence every man must be constantly on the look-out for contamination.

Mustard gas has great penetrant powers, whether as vapour, or as liquid; no ordinary clothing will keep it out for more than a few minutes, and if the skin is contaminated, defensive measures must be quickly taken if burns are to be prevented. If, then, troops on the march, or in attacking formations, may be sprayed with mustard gas, it appears a very difficult problem to arrange changes of clothing and decontamination in such circumstances. The Medical Services must expect to be called upon to treat large numbers of casualties, and to dispose of their contaminated garments and refit them.

Suppose, again, a gas attack is made from the air during disembarkation and concentration of a force, demands for hospital accommodation may prove far larger than those estimated for in the early stages of a campaign.

Before discussing the measures for meeting such situations, it is well to state the general position of the Medical Services as regards defence against gas.

Advice on protective measures against gas is not the function of the medical officer; this responsibility falls upon the officer commanding the formation or unit, and he will be advised either by specialist officers, or, in the case of units, by one of his own officers who has been specially trained at the Anti-Gas Wing Small Arms School. Of course, the medical officer, if commanding a unit, has the same responsibility in this respect as any other commanding officer, but the A.D.M.S. of a division, for instance, is not the responsible adviser of the G.O.C. in anti-gas measures.

We can now consider counter-measures against mustard-gas attacks.

Collective protection.—If chemical weapons are used from the air there will be need for constant vigilance so that the presence of gas may be recognized. This need emphasizes the fact that the gravity of the menace of chemical weapons is in inverse

proportion to the degree of discipline and training of the troops exposed to it. The history of gas casualties in units in the war makes this abundantly clear. Unfortunately, at present we have no simple chemical means suitable for use in the field for detecting mustard gas. The International League of the Red Cross last year offered a prize for such a detector, but the competition produced nothing of value. We have therefore to rely on sight or smell to detect mustard gas. As generally used in war, it leaves a dark stain, but it is by no means certain that this will always be so. At present the nose is our most reliable detector.

Every endeavour is being made to train troops to recognize the gas. In peace training it is not possible to use so dangerous a substance; we have, therefore, sought and found a relatively harmless substance which smells somewhat like mustard gas, and this is now used for training purposes.

Once contaminated, clothing and equipment must be rapidly disposed of and cleansed, and this is one of the most serious problems. In a war of movement the difficulties of getting large stocks of clean clothing to forward areas, and of cleansing that which has been contaminated, are very great. It seems to me that if gas is used in such circumstances against front line troops it is inevitable that large numbers will suffer from burns, since it will be impossible to provide changes of clothing before the damage is done. There are, however, certain individual protective measures which we will consider later. Some special organization will be necessary in order to deal with contaminated clothing and equipment, and at present the authorities are considering what form it should take.

There are several ways of getting rid of mustard gas, but if contamination is heavy, all demand fairly elaborate apparatus, which would be difficult to move further forward than railhead or some similarly organized post on the lines of communication. If the contamination is from vapour only, twenty-four hours' exposure in the open air in this climate is sufficient to render clothing safe to wear. This time can probably be considerably reduced in hot countries. Boiling for half an hour will also destroy gross contamination, and this is the method of election for oilskin protective clothing. All textiles can be decontaminated by steam ,but the process is elaborate, and in many cases, if the contamination is gross, it may be better to destroy the articles. For leather articles, for machinery, rifles, guns, etc., bleach is the best decontaminating agent. It can be used either as a powder, a paste, or cream with water, or as an ointment made up with petroleum jelly.

With the exception of exposure to air, all these methods demand fairly elaborate organization, and their use in forward areas is at least limited. If forward medical units receive large numbers of casualties, they will certainly have to dispose of large quantities of contaminated clothing and equipment for this purpose, and will have to be linked up with the cleansing units on the lines of communication.

Individual protection.—The respirator is a perfect protection for those parts of the body which it covers. Further, the modern respirator does not cause the discomfort and loss of efficiency of the war-time apparatus, and can be worn for hours without causing serious inconvenience. With highly trained troops, therefore, it should be possible to minimize the eye and lung casualties from mustard gas. To prevent skin burns is much more difficult. Mustard gas as liquid or vapour rapidly penetrates everything but air-proof fabric. Air-proof suits can only be worn for limited periods, even in temperate climates, and are useless in the tropics. We do employ them—ordinary naval oilskin is quite effective—for personnel engaged on special decontamination work, but only spells of work of about half an hour's duration can be undertaken without exhaustion. Several such spells can, however, be carried out in a day.

The Mark VII cape ground sheet affords good protection against penetration by mustard gas. With the shrapnel helmet, the ground sheet and the respirator, a fair amount of protection can be given. The addition of protective gloves and leggings is also contemplated.

All our efforts to find an effective and durable method of impregnating ordinary clothing to withstand mustard gas have up to date been unsuccessful.

If contamination occurs it must be quickly removed, or burns of varying degree, depending upon the concentration of the poison and the length of exposure, will result. Soap and water is effective, but the scrubbing must be thorough and prolonged. A more practical preventive for front-line units is bleach ointment. This is made up with equal parts of bleaching powder and petroleum jelly. The mixing must be thorough. In temperate climates if this ointment is applied to the contaminated skin within five minutes, even very gross contamination with liquid mustard can be neutralized, and no burn will result. The ointment has not so far proved so successful in hot climates, but further experimental work is being carried out. The ointment does its work with a very short period of contact—three to five minutes—and we have found that even repeated applications for short periods do not cause dermatitis.

From this brief survey it will be seen that, though the danger from mustard gas is serious, particularly if used from air weapons, much can be done to lessen it, particularly with highly-trained troops who have been taught to recognize the poison.

The problem of mustard gas is similar to that of malarial prevention, as we met it in the eastern theatres of war. Casualties are inevitable, and there is no panacea for prevention, but intelligent application of known preventive measures, with strict training and discipline, will minimize them.

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Discussion.—Dr. C. M. WILSON related his experiences of gas attacks in the early stage of the war, and pointed out the effect of gas shock combined with trench fatigue; he showed that after a short experience of this means of attack, the percentage of serious cases was very low.

The PRESIDENT mentioned the steps which the Royal Red Cross Society were taking to instruct the civil population against possible gas attacks.

Section of Otology.

President—Mr. NORMAN PATERSON, F.R.C.S.

[*February 5*, 1932.]

Aural Vertigo.

By W. S. THACKER NEVILLE, M.D., F.R.C.S.Ed.

TO-DAY I am supporting the theory of Dida Dederding of Copenhagen—that symptoms of deafness, tinnitus and vertigo with vomiting and diarrhœa, may be due to a faulty water metabolism. I do not mean to exclude other causes, for I can quote a severe case of vertigo and deafness which was cured by a tonsillectomy and another patient who was cured by the extraction of a tooth.

The fact that these symptoms may be due to a faulty water metabolism, demands that we should test such a patient's water metabolism. The signs that would lead us to carry out these tests in a patient with the symptoms of deafness, tinnitus and vertigo, are:—Variability in the deafness and tinnitus, raised lower limit, absent or diminished bone conduction for a_1 435 d.v. and normal high limit in early cases.

Spontaneous nystagmus is present in patients if seen during or a few days after an attack, and according to Dederding may be rendered evident by the inhalation of amyl nitrite.

Further signs are thickness of the skin over the calves of the legs and at the back of the neck, headache, rheumatism and local infiltrations of the skin.

Labyrinth tests show a different reaction between the two ears to the turning test corresponding to a latent spontaneous nystagmus; the caloric reaction only shows a reduced or absent reaction in advanced cases, whilst the galvanic test is normal.

I carried out labyrinth tests for the purpose of this paper, but I believe it is unwise to subject such patients to these tests, as the variability in the deafness and tinnitus and the absent or diminished bone conduction are sufficient indications for carrying out the water metabolism tests.

The pathology is said to be overloading of the whole body, especially the labyrinth, with fluid. Thus, the increase in weight is due to retention of water in the tissues as are also the subcutaneous infiltrations at the back of the neck and in the legs. These abnormal deposits of water in the labyrinth may produce displacement of the stapes, and hence aural phenomena; œdema of the meninges produces headache; œdema of the mucous membranes results in stenosis of the Eustachian tube; and œdema of the muscles and fasciæ produces rheumatism.

The variability in deafness and tinnitus is due to a variable intake and loss of fluid. This variability can be seen during the water test, when a patient will complain of increased tinnitus, deafness, and giddiness, on drinking the 1,000 c.c. of fluid which we administer.

Unless the patient shows a faulty water metabolism, it is of no use treating the disease on that basis. The faulty water metabolism is demonstrated by asking a patient to drink 1,000 c.c. of water and measuring the output for four hours. A normal person passes 1,000 c.c. or more. An abnormal person will pass 500-600 c.c. and will increase in weight corresponding to the amount of retained fluid. Thus, if the patient passes 500 c.c. he ought to be 500 cgm. heavier. As a matter of fact, he will only be 250 or 300 cgm. heavier, as he loses a certain amount of fluid through the skin and lungs that is not measured in the output from the kidneys.

The second test, which also initiates the treatment, consists in giving intravenously 1 c.c. of the powerful diuretic, salyrgan. This produces a diuresis in both the normal

and abnormal individual on the day following the injection, but the normal individual has a correspondingly diminished output on the second day, whilst the water-logged individual will show an increase over the normal output on the second day as well as on the first day.

The third test is to estimate the percentage of hæmoglobin, as many of these patients show only 75%.

The treatment is life-long and consists in a no-salt diet, limited intake of water (sometimes even to one pint a day), increased output of water, via the skin by Turkish baths, via the lungs and skin by exercises and massage, via the kidneys by intravenous salyrgan, to commence with. Mild diuretics always make the patient worse.

If a patient does overstep the mark as regards fluid, I have found that bulbocapnine may arrest the symptoms. If given hypodermically, it acts in from five to fifteen minutes, whilst if given by the mouth it acts more slowly. Bulbocapnine does not suit some patients, as it leads to mild prostration and bursting headache.

Recently I have been able to demonstrate the action of bulbocapnine on the labyrinth. A patient, aged 14, had acute labyrinthitis. His vomiting continued for two days. On the evening of the second day I gave him 0·5 grm. of bulbocapnine. Almost at once the vomiting ceased, so that he was able to retain fluids by mouth; his giddiness decreased, though the nystagmus was still evident.

If a patient is unable to take bulbocapnine, one must resort to atropine or ergotinine.

Illustrative Cases.

(I) A. H., male, aged 52, complains of intermittent deafness of three years' duration, tinnitus, which varies in loudness, and giddiness which consists of everything appearing to go round from right to left, followed by vomiting and diarrhœa. Patient's former weight was 10½ st.; it is now 12 st. 7 lb. He has pain in front of the legs and knees and over the biceps, and this prevents him from taking exercise. He has suffered from cold feet for over two years and does not perspire. There are raised red patches on the right thigh.

On examination.—The skin at the back of the neck and calves of legs is thickened. Both tympanic membranes are greatly retracted. Teeth, absent. No sign of infection in nose or throat. The affected left ear showed a raised low limit 128 d.v. Air conduction (a_1 66 = 18) and bone conduction decreased (a_1 15 = 8). High limit lowered (monochord 11943).

Rotation to the right produced nystagmus for twenty seconds without giddiness; rotation to the left produced nystagmus for twenty-five seconds with giddiness. In the Babinski-Weil test the patient walked towards the right, i.e., towards the unaffected ear. Response to the galvanic test was normal. Water metabolism showed a retention of 600 c.c. The salyrgan test showed increased output over forty-eight hours.

Treatment with a limited fluid intake and no salt shows after the interval of a month air conduction for a 60 in. watch was increased from 6 in. to 54 in., the low limit lowered to 32 d.v. from 128 d.v. air conduction for a_1 increased from 18 seconds to 39 seconds, and bone conduction increased from 8 seconds to 30 seconds.

(II) Miss B., aged 47. Vertigo began in December, 1930, whilst patient was drinking quantities of barley water in order to cure sciatica. January, 1931: Nausea, vomiting, giddiness and diarrhœa. When vomiting is over, giddiness is diminished. 11.8.31.—Complained of deafness and tinnitus in right ear. *On examination.*—The affected right ear showed a raised lower limit (72 d.v.); air conduction decreased ($a_1$66 = 22″); bone conduction was absent ($a_1$15 = 0) and high limit lowered (C_4 = − 15″).

Rotation to left produced no nystagmus; rotation to the right produced nystagmus for 25 seconds. Cold caloric test: right ear, nystagmus lasting 2 seconds; left ear, nystagmus lasting 35 seconds and nausea. The water metabolism test showed a retention of 300 c.c. The administration of water produced giddiness and tinnitus.

The salyrgan test showed an increased output over forty-eight hours. Treatment by no-salt diet and limited fluid intake resulted in a cure of all the giddiness except for a feeling of weight in the head and a tendency to walk to the left, which was cured by atropine per os

and a leech on the mastoid. Hearing tests showed low limit lowered from 72 d.v. to 32 d.v. Bone conduction increased from 0 in. to 14 in.

(III) Miss L., aged 45, complains of room going round, sensation of falling to left, headaches which are greater when the attack comes on. The affected right ear showed raised low limit (202 d.v.), decreased air conduction ($a_1 66 = 7''$), slightly decreased bone conduction ($a_1 15'' = 12''$), high limit lowered ($C_4 = -15''$). A water metabolism test showed 427 c.c. retention. Treatment consists of limited fluid intake, no salt and calcium diuretin gr. 15 t.d.s.

A month later the patient wrote to say that she had been free from any bad attacks.

(IV) H. W. B., male, aged 42, came to me in November, 1929, with otitis media and tinnitus. The otitis media was cured by ionization. 17.10.31.—Deaf to shouting voice and all tuning forks. Gave history of drinking ten pints of fluid a day. I gave him an intravenous injection of salyrgan and put him on a pint of fluid a day and no salt. The result on 24.10.31 was that he could hear conversational voice. A water metabolism test showed a retention of 595 c.c. This patient, although he was deaf owing to drinking too much fluid, was not giddy, because his labyrinth had been destroyed by old otitis media; the rotation and caloric tests failed to produce nystagmus, but the galvanic test produced nystagmus with 5 m.a.

I have not shown any cases that have been benefited by bulbocapnine, but I have patients who constantly take it. One is a man aged 84, who was confined to bed and displayed a strong nystagmus and response to tuning-fork tests typical of a faulty water metabolism. His water metabolism was not tested. I ordered limitation of fluid, no salt and bulbocapnine and I heard that he was soon able to walk about and that he keeps perfectly fit, unless he oversteps his limited fluid intake when he resorts to bulbocapnine.

Another patient is a man, aged 48, who suffered from violent attacks of vertigo and vomiting. Tuning-fork tests reveal advanced nerve deafness. The labyrinth tests show nystagmus 30″ on turning to the right or left but no giddiness. Cold caloric 10 c.c.: no reaction in right ear and momentary nystagmus in the left ear; 60 c.c.: momentary nystagmus in the right ear. Galvanic test 14 ma.: no nystagmus.

This patient always carries three tablets of bulbocapnine, as the drug prevents a severe attack of vertigo. He has also been much benefited by a no-salt diet and limited fluid intake, though his water metabolism was not tested, as he visited me before I employed these tests. He was placed on a limited fluid intake and no salt because he told me he was increasing in weight rapidly.

(V) Finally I show charts from a case of aural vertigo in which there was not a faulty water metabolism. [Charts exhibited on screen.] The low limit was raised to 101 d.v. Air conduction decreased ($a_1 66 = 20''$); bone conduction increased ($a_1 15 = 33''$) and high limit was lowered ($C_4 = -15''$. $C_5 = 0$). Response to caloric and galvanic tests normal. Neither the water metabolism nor salyrgan tests showed retention. Acoustic tumour was excluded by the findings of the neurologist and the radiologist and by the normal response to the caloric test, so as the vertigo had lasted for five years I performed a Neumann's labyrinthectomy.

Discussion.—Mr. F. W. WATKYN-THOMAS: The most important advances in the treatment of Ménière's syndrome since it was first described, have been the work of Mr. Sydney Scott on the effects of Eustachian obstruction, that of Portmann on the vascular factors, and on the saccus endolymphaticus, and that of Mygind and Dederding on water retention.

In the first place, if we use the term "Ménière's syndrome" at all, we must use it in its original sense, i.e., vertigo associated with changes of hearing coming on as a sudden attack, a sense fully covered by de Kleyn's definition—"a sudden alteration of the activity of the auditory nerve in its cochlear and vestibular portions." For practical purposes we are entitled to make two reservations: (1) We may exclude all those cases in which the symptoms are due to labyrinthine suppuration, or to any localized intracranial lesion. (2) In the majority of cases we are concerned with recurrent attacks of these symptoms.

If we attempt to make our definition more precise, for instance, by specifying the changes of hearing, we limit ourselves to a group of Ménière cases, and we are only entitled to speak of observations on these cases as observations on a strictly limited group, not as observations

on Ménière's syndrome as a whole. I particularly emphasize this, as I do not think any one of the investigators whom I have mentioned claims that his results apply to all cases of Ménière's syndrome. The results of treatment are, in fact, to some extent mutually exclusive. Thus we know that many cases are cured by Eustachian inflation alone, a method based on the assumption that the labyrinthine tension has been raised by the in-driven stapes, whereas Mygind and Dederding have cured many other cases by a method based on the assumption that there is labyrinthine hypertension, which must force the stapes outwards.

One point is of interest here. I do not think water-retention cases are nearly so common in this country as they are abroad. Whenever I have visited Dr. Mygind's clinic I have seen several undeniable cases; here, either in private practice or in hospital, I have seen very few. It may be to some extent a question of diet; for one thing, I do not think we consume as much salted foods as the more northern countries.

There is another point. All the researches to which I have referred show that the most frequent cause of a Ménière attack is an intermittent, unilateral increase of labyrinthine pressure, either by in-driving of the stapes (Scott), excess of endolymph by failure of excretion (Portmann), intracellular labyrinthine œdema (Mygind), or alteration of blood-volume (Portmann). It is probable that the vertigo associated with accessory sinus infection is really secondary to relapsing Eustachian catarrh kept up by that infection.

There must be another group of cases, a small group certainly, but one which undoubtedly exists. I refer to those cases which defy all Eustachian therapy and are cured by small doses of luminal or bulbocapnine. Here we must admit some cause other than raised intra-labyrinthine pressure.

We do not here consider the so-called Bárány syndrome, for that is a posterior fossa lesion and can operate, as several of us have shown, in the presence of an inactive auditory nerve.

In conclusion, I must repeat that in no way do I attempt to depreciate this most important work. The researches of Mygind and Dederding, for example, have far wider implications than Ménière's syndrome; I only wish to reaffirm a belief that Ménière's syndrome is a syndrome, not a pathological entity.

Mr. EDWARD D. D. DAVIS: For the purpose of the discussion on aural vertigo at the British Medical Association Meeting at Eastbourne, I went through the notes of 76 of my cases of aural vertigo with the object of ascertaining the causes from a clinical point of view. I did not recognize any cases of water-logging, and though I saw a few cases in which depletion therapy had been carried out and bulbocapnine administered, the results were indifferent.

The following is a list of the clinical causes of the vertigo in the 76 cases:—Traumatism, 3; acute otitis media, 3; acute suppuration of exacerbation of a chronic suppuration, 5; chronic suppuration, 12; secondary sclerosis or healed suppuration, 14; Eustachian obstruction (?), 2; otosclerosis, 14; cerebellar abscess, 2; tabes, 2; disseminated sclerosis, 3; general (intestinal and circulatory), 3; cause unknown, 12. Total, 76.

The twelve cases of unknown cause were in middle-aged or elderly patients, thin, worried and overworked, who complained of severe rotary vertigo of sudden onset, and of tinnitus. The range of hearing in one ear was much diminished, especially for high notes. These cases would be labelled Ménière's disease. The labyrinth was active to the irrigation test, but in a few cases the reaction was sluggish. Vomiting he interpreted to be only an indication of the severity of the vertigo, and the same with regard to diarrhœa. In the later and milder attacks of vertigo there was no vomiting. The Eustachian tubes were clear, and the blood-pressure normal. The vertigo was very variable, and the pathology of these cases is definitely obscure.

If the auditory nerve could be seen with the ophthalmoscope or similar instrument, we should probably know more about vertigo and nerve deafness. The analogy with the eye may be carried still further, and cases of increased intra-labyrinthine pressure may be compared to glaucoma. The ophthalmologist has the advantage of being able to measure the intra-ocular pressure with a delicate gauge known as the tonometer, and so verify the effect of any treatment for the reduction of pressure. Depletion therapy for glaucoma was tried in 1915, when these patients had been given an intravenous injection of saline, as in cases of cerebral compression. This treatment has been given up as unsatisfactory, but it was found that there was a decrease in the intra-ocular pressure for twelve hours only. Perhaps one reason for giving up depletion therapy in glaucoma was the need for mental

relaxation and quiet. The same applies to vertigo. If a patient is given such a potent diuretic as salyrgan he is in and out of bed every five minutes with considerable disturbance of sleep.

With regard to lumbar puncture, Bakinski in 1903 performed lumbar puncture for vertigo of functional origin, and claimed good results, particularly when no lesion of the ear was apparent. I have tried lumbar puncture in some of the above patients; the cerebrospinal fluid was normal, and the condition was not improved.

Portmann's operation for drainage of the saccus endolymphaticus has been performed with success by Mr. Musgrave Woodman. Patients with vertigo do not readily consent to operations, and seem to prefer the vertigo to anything but simple treatment. The evidence of increased intra-labyrinthine pressure or of water-logging in the above cases was absent.

In the fourteen cases of otosclerosis there was severe vertigo, but it was temporary, and disappeared with rest and the administration of bromides. These patients were usually sea-sick, train-sick, anxious women, with normal patent Eustachian tubes. In most cases of otosclerosis the blood-pressure is normal; in a few it is depressed and low. In these latter I have tried Mr. Richard Lake's treatment with ergotin without much success. The low blood-pressure is probably partly due to the vertigo, but the question of blood-pressure needs more careful investigation.

The secondary sclerosis cases are those for which one might perform labyrinthotomy, especially when a previous radical mastoid operation has been performed. Such operations are justified: (1) if it is certain that the vertigo is due to the ear; (2) when all other remedies have failed, and (3) if the patient is incapacitated by the vertigo. The cases which fulfilled these three conditions are few; Richard Lake records only 14.

The cases of acute suppuration or exacerbation of a chronic suppuration are the most satisfactory, and the vertigo usually disappears when a mastoid operation is performed.

Mr. Thacker Neville has mentioned some cases of acute otitis media with vertigo. I have seen three patients of this type; when the otitis cleared up the vertigo disappeared and did not return.

In the three traumatic cases the vertigo was probably due to cerebral disturbance, and not caused by the ear.

Mr. A. W. McCay: In 1926, at the request of Mr. J. S. Fraser, I made an investigation into the cases of Ménière's symptom complex, dating from the year 1908 to 1926.

One of the greatest difficulties was the classification of the cases. In all, there were 199 cases of Ménière's symptom complex, and of this number I have chosen 28, which I consider are cases of true Ménière's disease (excluding all cases with suppurative conditions, such as labyrinthitis), etc.

To-day I intend to confine my remarks chiefly to these 28, except for a brief classification of the remaining 171. In these 28 cases, which I consider to be cases of true Ménière's disease, the membrana tympani were normal in appearance, the Eustachian tubes were patent, and there was a history of sudden onset of severe giddiness and tinnitus, accompanied by deafness in the affected ear and vomiting during the attack. In each case, the hearing tests showed inner-ear deafness, with raising of the lower tone-limit in all and slight lowering of the upper tone-limit in most cases. The cold caloric test in each was more or less normal, that is, the reaction was present within thirty seconds. The deafness was unilateral in 19 cases and bilateral in 9, but in these latter cases one ear was always more affected. There were 17 males and 11 females. The greatest age-incidence was over 40 years of age, there being only 10 cases under this age. In many of the cases there had been a history of tinnitus and symptoms of deafness for some considerable time prior to the onset of the giddiness and vomiting, and in the cases where observation had been made over a period, it was clear that the deafness was progressive.

The remaining 171 cases showing Ménière's symptom complex, that is, severe attacks of giddiness accompanied by deafness and noises in the ear, no sickness, but of apoplectic origin, were classified as follows: Traumatic in origin, 33; toxic neuritis or chronic progressive labyrinthine deafness, 32; syphilitic neuritis eighth nerve and labyrinthitis, 71; tumours of the eighth nerve, cerebello-pontine angle and cerebellum, 20; vascular and anæmic, 15. Total, 171.

It is important to define clearly the type of case with which we are dealing. As we know, Ménière's syndrome can be caused by a plug of hard wax in the external auditory meatus, by an acute otitis media, labyrinthitis, tumour of the auditory nerve, etc., but where the pathology of the condition is known, I do not think it ought to be termed Ménière's disease,

otherwise we are dealing with symptoms of a known condition, whereas, Ménière's disease seems to me to be in the same parallel as migraine, asthma, and epilepsy, and thus until we know the definite pathology of these cases, the treatment will always be baffling.

As regards treatment, I find that in severe cases complete rest in bed for two or three weeks, a strictly limited diet, and small doses of calomel, together with luminal and bromides, give definite relief.

Mr. HUGH CAIRNS asked whether Mr. Thacker Neville had seen Ménière's syndrome in severe water retention, such as the œdema accompanying various forms of nephritis. If the pathology of the condition was really water-retention, one would expect to get it also in kidney cases. He had been interested in Ménière's syndrome recently because cases had been sent to him for division of the eighth nerve. Dandy introduced that operation and had reported successes. His (Mr. Cairns') own cases were too recent for him to say anything about the late results, but the immediate results of the operation were satisfactory, and the operation was fairly easy to perform. It should be limited to cases in which there was gross loss of hearing in one ear.

Mr. H. V. FORSTER said that having observed, in his student days, that his ability to hear clearly through the stethoscope during auscultation of the heart and chest, varied with regard to lower tones, he found that he could test his own ear for low tones in a simple manner by firmly closing the external meatus with the index finger upon the tragus, when under normal conditions the muscle note or muscle tone set up by the contracting muscle of the hand or forearm could be heard. When this failed to be appreciated, which was found to be the case in his right ear, he concluded that the lower tone hearing limit had been raised.

On one occasion he experienced a slight but very disagreeable attack of vertigo referred to the right ear, and discovered on another occasion that the temporary loss of hearing for low tones completely disappeared after an attack of vomiting of a copious amount of fluid.

It was not until he had seen some of the writings of Dederding and Mygind, and also those of Mr. Thacker Neville, that he felt satisfied that his own personal experiences could be explained by the hypotheses of those writers.

It should also be mentioned with regard to hearing tests in which the method of closing the tragus was used, that Federici,[1] of Genoa, had recently described a test in which after the 128 d.v. fork had ceased to be heard on the mastoid by bone conduction it could be heard for a considerable period with its base applied to the closed tragus, but in cases believed to have stapes fixation, e.g., in otosclerosis, this period was remarkably shortened.

Dr. KERR LOVE said that the cases described in the paper bore a superficial resemblance to cases of hypothyroidism and he would therefore ask whether Mr. Thacker Neville had tried administering thyroid tablets for the relief of the swelling and the kidney condition.

Mr. E. WATSON-WILLIAMS said that since he had not himself observed the condition described by Mr. Thacker Neville, he must confine his remarks to theoretical considerations. The treatment outlined seemed very drastic even for a month, and as a régime for a lifetime hardly compatible with existence. It was important, therefore, to be certain that the attack on the faulty water metabolism was the only or the best line of treatment. Surely there must be some aural lesion in addition, for if both ears were normal it was difficult to understand how a symmetrical plethora should cause vertigo. Was Mr. Neville not himself giving bulbocapnine for its effect on the vestibular nerve-endings or possibly on the cortex? He (the speaker) was accustomed to rely on small doses of quinine for controlling vertigo of this type. Another drug that he had found effective, especially when there was also tinnitus, was mercury; from ten to twenty minims of the liquor hydrargyri perchloridi twice a day were sufficient, and caused no alimentary disturbance.

Mr. W. STUART-LOW said that one of the cardinal principles to observe in cases was rest in bed and quiet. Bromides with drachm doses of dilute hydrobromic acid in the case of middle-aged and elderly patients, particularly women, were beneficial and soothing, but for younger women and girls, luminal in half-grain doses, increasing the dose to one grain every three hours, often proved useful. Quinine in half-grain doses acted as a tonic to the vestibular branches of the auditory nerve and so helped to steady the patient.

[1] *Acta Oto-Laryngologica*, xvi, Fasc. 1, "A new test mainly for determining the presence of Ankylosis of the stapes at the oval window."

Dry-cupping by placing medium-sized cups over the region of the mastoid and round to the middle line at the back on the affected side greatly helped by drawing blood more or less directly from the congested area of the labyrinth. The application could be maintained by making use of a suction pump for five minutes at a time and repeated at intervals of ten minutes for a few times.

He had found small repeated doses of liquor hydrargyri perchloridi in mixture, and calomel in pill, most effective in lowering the blood-pressure by freely acting on the liver and bowels.

He considered too great restriction of the intake of fluids undesirable, as the cause of the vertigo might be toxins circulating in the blood, and their elimination, being essential, was best accomplished by giving water freely, especially in the early morning, while restricting fluids only throughout the day.

Mr. ALEX. R. TWEEDIE said he ventured to suggest that Mr. Neville had emphasized the factor of water metabolism unduly; in support of this suggestion he would quote some extracts from the actual summary by Dr. Dederding, of the reports just mentioned—as follows:—

"By m.b. Menièri we understand a disease which, as far as the ear is concerned, is characterized by changing acoustic and vestibular abnormalities, and which has no specific etiology. The acoustic function is generally affected on both sides. The great majority exhibit abnormalities of the tympanic membrane. Tubal stenoses are frequent. The elevated lower limit indicates an affection of the sound transmitting apparatus. The generally well preserved upper limit speaks against a presumption of an affection of the sound perceiving apparatus."

He (the speaker) objected to the term "m.b. Menièri," but these statements by Dr. Dederding accorded well with his own small experience of cases of vertigo which he had examined.

It was important, primarily, not to regard vertigo as a mystery. Everyone experienced these symptoms more or less and their recognition varied largely accordingly to the psychic conditions. Vertigo could be easily induced, as all knew, by rotation, but if a child were vigorously rotated, he would get up and run away laughing, whilst one or two slow turns could induce extreme discomfort in an elderly person.

He urged that, as indeed Dr. Dederding's summary stated, there was always some demonstrable underlying middle-ear lesion, and as far as his own examinations were concerned there was also a demonstrable asymmetry of both the vestibular and the auditory functions. Such functions, however, on each side might still be within the physiological limits, but the essential point was asymmetry. Such underlying conditions may well have been present many years, but it was not until some other influence occurred, such as the effects of constipation, an over-loaded stomach, unaccustomed stooping, or e.g., the menopause, that this asymmetry became "recognized" by the patient.

The symptoms, he admitted, might be most alarming; more than one case had been referred to him as possibly due to cerebellar tumour.

With regard to treatment: the right line was encouragement, with the assurance of the patient that the symptoms really only represented such "recognition" of an old-standing trouble and to which they would soon become accustomed. He would also urge general tonic treatment and avoidance of sedatives; in his experience with this form of therapy recovery was not long delayed.

Sir JAMES DUNDAS-GRANT said that Dida Dederding's definition of Ménière's disease was somewhat vague. The rationale of small doses of quinine in aural vertigo was that it had an anodyne effect on the vestibular nerve. The effect was to produce, not a weakening of the affected side, but a lowering of the hyperactivity of the sound side, because, as Mr. Tweedie had remarked, there was an asymmetry between the two labyrinths, an important element in the production of Ménière's symptoms.

In cases of otosclerosis probably the reason of the vertigo was that, one of the windows being quite closed, as say in fixation of the stapes, there was not the safety-valve action which the movement of the stapes would allow and vascular or other changes in pressure were not compensated.

Nothing had been said to-day about the post-suppurative adhesive changes which were so frequent in the cases of aural vertigo sent to him. He (the speaker) had, for instance, found a severe attack to have been due to the "indrawing" of a small loose cicatrix. When this was sucked out and fixed with collodion the patient was quite comfortable.

He hoped that Mr. Thacker Neville was making use of his (the speaker's) cold-air apparatus. Monrad-Krohn, in his book on the examination of the nervous system, stated that he had given up cold-water tests and was now using this cold-air apparatus.

With regard to the discomfort of a no-salt diet, he, Sir James, after adopting such a diet had been able to detect new flavours in his food, and he held out this fact as a grain of comfort to those who found the absence of salt a great deprivation.

Mr. THACKER NEVILLE, in reply to Mr. Davis, said he had treated one case of vertigo with acute otitis media and had cured the otitis by ionization. The hearing was not fully recovered nor was the vertigo cured until the source of the toxæmia, namely, septic tonsils, was removed. Most cases of water-logged patients in Copenhagen were also treated with the Eustachian catheter in order to rectify the position of the stapes which was displaced by the negative pressure due to the water-logging of the Eustachian tube. I myself did not use it in this investigation in order to show the effect of limited fluid intake.

In reply to Mr. McCay: with this treatment rest was not necessary as the patient could be quickly depleted of fluid and therefore exercise was demanded in order to make the skin active.

Mr. Hugh Cairns had asked why people with nephritis did not have aural vertigo. The reason was that nephritis was intercellular, but this water-logging was an intracellular accumulation of fluid and there was no pitting. Dandy had reported eleven cases of division of the eighth nerve, nine of which were claimed as cured. For him (the speaker), this would be a dangerous operation, but destruction of the labyrinth was not dangerous. Furthermore, the destruction of the vestibular branch was not sufficient, as tinnitus was an annoying symptom which could only be rectified by destroying the cochlear branch of the eighth nerve or the cochlea itself. If a patient was water-logged such radical operations were not necessary.

Dr. Kerr Love had mentioned the treatment with thyroid. The patient, who was deaf and had been drinking ten pints of beer a day, found it impossible to limit fluid intake to one pint, therefore he took tablets of elityran which was tenfold more effective than thyroxin and said he had received great benefit from it. All other patients placed on elityran were rendered worse.

Mr. Watson-Williams had asked whether there was no other method besides the unpleasant one of limitation to one pint of fluid daily. Anything which caused loss of fluid—such as dancing—was useful. Mr. Watson-Williams mentioned the difficulty of understanding why one labyrinth only was water-logged; he (the speaker) believed that actually both labyrinths were water-logged, but as the vertigo was always preceded by deafness, the increased pressure in the labyrinth would displace the stapes in the deaf ear, whilst in the healthy ear there would not be such a displacement.

The action of bulbocapnine on the labyrinth was shown by its power of arresting vomiting in a case of acute labyrinthitis.

Mr. Stuart Low had referred to the usefulness of leeches. He (Mr. Thacker Neville) had found their application successful in one water-logged patient who, although the giddiness was cured, yet at times had a sensation of a weight on her head and a feeling of being compelled to walk to the side of the affected ear. A leech on the mastoid removed this sensation for three weeks at a time.

Mr. Tweedie had mentioned the necessity of performing labyrinth tests. Labyrinth tests had been carried out in most of the cases which he had reported. The reason why he had said they were inadvisable was that the patients found them unpleasant. Those he met with had suffered from severe giddiness; one had broken her wrist and another had been thrown out of his chair and was unable to drive a car. The abnormality in the rotation tests could be accounted for by a latent nystagmus. The caloric test showed a greater difference between both ears, whilst the response to the galvanic test was normal.

He thanked Sir James Dundas-Grant for his recommendation of his cold-air apparatus, which was essential as it would prevent acute otitis following the caloric test in the case of a patient with a perforated tympanic membrane.

The Pathology of Deaf-Mutism.

By J. S. Fraser, M.B., F.R.C.S.Ed.

(From the Laboratory of the Royal College of Physicians, Edinburgh.)

Probably the best method of classifying cases of deaf-mutism is to divide them into: (1) those due to an error in development (Constitutional or Congenital Deaf-mutism); and (2) those due to inflammatory conditions (Inflammatory or Acquired Deaf-mutism), though it must be admitted that a sharp boundary line between these groups cannot always be drawn.

(1) Under developmental or congenital deaf-mutism there are two groups: (*a*) the sporadic form, well known in this country; and (*b*) the endemic form, frequently seen in Switzerland.

(2) The inflammatory or acquired variety includes cases due to (*a*) traumatism; (*b*) congenital syphilis; (*c*) meningitic labyrinthitis; and (*d*) labyrinthitis following otitis media.

(1) (*a*) *Sporadic congenital deafness.*—In this there are four subgroups:—

(i) Aplasia of the whole labyrinth (Michel's type) is very rare and is probably due to non-formation of the otic vesicle in the first month of fœtal life.

(ii) Malformation of the bony and membranous labyrinths (Mondini's or Alexander's type). The bony capsule of the cochlea is flattened from base to apex and the normal arrangement of the scalæ is only present in the basal coil. In the upper part there is a wide common space. Corti's organ may be absent or may show an embryonic form, while the cochlear ganglion is situated centrally in the modiolus and does not take a spiral course. The condition corresponds to that seen in the lowest mammals, the duckmole and echidna. A similar condition of the cochlea is seen in the second and third months of fœtal life. The development of the cochlea takes place from base to apex, so that if development is arrested at a certain point, the septa between the higher scalæ fail to form, and consequently we have the production of a wide space (cloaca) at the apex of the cochlea.

Figs. 1, 2, 3 and 4 are from a case of congenital deaf-mutism in an idiot boy. They show almost total absence of labyrinth of the left ear (figs. 1 and 2)—a condition approximating to Michel's type—and deformity of the cochlea of the right ear (figs. 3 and 4)—Mondini's or Alexander's type of congenital deaf-mutism.

(iii) Malformation affecting both the cochlear and vestibular apparatus. This form is said to be associated with retinitis pigmentosa and feeble mental development. The vestibular reactions are greatly diminished or absent, and the patient's gait is uncertain. The most marked features on microscopic examination are hypoplasia of the sensory epithelium in both parts of the membranous labyrinth, atrophy of the cochlear and vestibular ganglia, alterations in the blood-vessels and changes in the brain. The conditions found in the labyrinths of waltzing mice are somewhat similar to those described above. (No specimen.)

(iv) Sacculo-cochlear malformation (Scheibe's type). About 70 per cent. of cases of congenital or developmental deaf-mutism belong to this type, in which the utricle and canals (pars superior) are intact and the vestibular apparatus reacts normally to rotation and caloric tests. Hearing remnants are often present. On microscopic examination the saccule and cochlear canal (pars inferior) are usually collapsed but may be abnormally dilated. Corti's organ is as a rule absent in parts and in others malformed. The membrana tectoria does not reach the malformed Corti's organ but in some places is tucked into the internal spiral sulcus, while in others it is attached across the scala media to the stria vascularis. The stria itself may form a polypoid projection. The spiral ganglion is usually atrophied.

Figs. 5, 6, 7 and 8 are from a case of congenital deaf-mutism of Scheibe's type in which the cochlea and saccule are malformed but the vestibular apparatus is

normal. Figs. 5 and 6 are from the left ear and show dilatation of the cochlear canal, extreme malformation of Corti's organ, membrana tectoria attached to stria vascularis (fig. 5) and membrana tectoria lying on Hushke's tooth (fig. 6). Figs. 7 and 8 are from the right ear of the same patient.

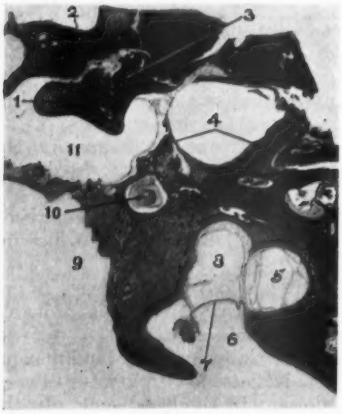

FIG. 1.

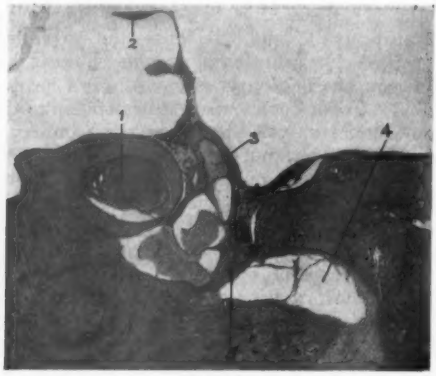

FIG. 2.

FIG. 1.—From a case of congenital deaf-mutism in an idiot boy. Horizontal sections through left ear, No. 52. × 4 diam. 1, Incus. 2, Outer wall of aditus. 3, Malleus. 4, Tensor tympani tendon and muscle. 5, Basal coil of cochlea? 6, Internal meatus (note absence of cochlear nerve). 7, Dura mater in fundus of meatus. 8, Probably perilymph space of maldeveloped cochlea. 9, Posterior fossa: normally this position would be occupied by the vestibule. 10, Facial canal. 11, Internal attic.

FIG. 2.—From same case as Fig. 1. Horizontal section through left ear, No. 110. × 12 diam. 1, Facial nerve. 2, Incus. 3, Anterior crus of stapes (note that the posterior crus is adherent to the facial canal). 4, Vestibule. 5, Deformed footplate of stapes.

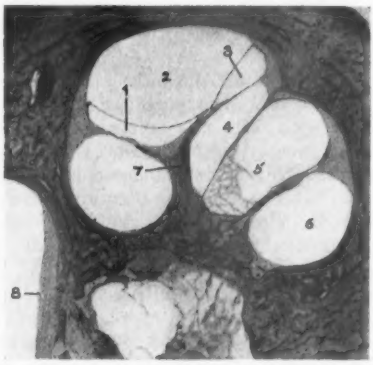

FIG. 3.—From same case as Fig. 1. Right ear, Section 234. × 12 diam. 1, Scala media of upper part of basal coil. 2, Cloaca. 3, Cochlear canal, and 4, Scala tympani of the rudimentary middle coil. 5, Scala vestibuli of lower part of basal coil (note remains of embryonic connective tissue). 6, Scala tympani. 7, Rudimentary modiolus. 8, Lower part of saccule.

Figs. 9, 10, 11 and 12 are from a congenitally deaf white bull terrier. Note that congenital deafness and albinism are often associated.

(1) (*b*) *Endemic or cretinic deafness* (*Siebenmann's type*).—According to Nager the average number of deaf-mutes in Europe is eight in ten thousand, but in

Switzerland it is twenty-four in ten thousand. In more picturesque language, it has been said that deaf-mutism in Europe diminishes from the Alps towards the sea.

Stein states that 25% of cretins have normal hearing, 45% slight deafness, 25% severe deafness, and 5% absolute deafness. Nager gives the following figures: among cretins there are 29% of deaf-mutes and 32% hard of hearing.

Microscopic examination of the ear shows myxomatous thickening of the submucous tissues of the middle ear often filling up the window niches. The tympanic cavity may even be obliterated. In one of Nager's cases the malleus and incus were deformed and the long process of the incus and the head and posterior limb of the stapes were adherent to the facial canal (fig. 13). There may be thickening of the footplate of the stapes, or even bony ankylosis to the margins of the oval window. The whole wall of the promontory may show hyperostosis (fig. 14). Endostoses have been reported growing into the hollow spaces of the cochlea, vestibule and canals, with resulting deformity of the scalæ, &c. Few writers have reported any

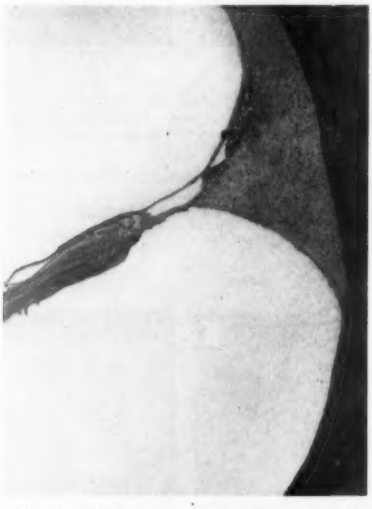

FIG. 4.—From same case as Fig. 1. Right ear. Section 234. × 50 diam. Showing scala media of basal coil, which is collapsed. Corti's organ and membrana tectoria are rudimentary but the stria vascularis and the spiral prominence are well formed.

gross abnormality in the labyrinth itself, but in one of Nager's cases the cochlear duct was dilated in the lower and collapsed in the upper part. Alexander found marked degenerative changes in Corti's organ. The vestibular apparatus is normal. Nager states that the condition arises about the sixth month of fœtal life and continues even after birth.

According to Nager, tuning-fork tests show that many cretinic deaf-mutes are really only hard of hearing. This degree of deafness, however, in conjunction with the feeble mental development of the patient, results in deaf-mutism. Nager further states that the deafness is not always due to defects in the ear but may be caused by changes in the cerebral cortex.

Figs. 13 and 14 are from microscopic slides from cases of endemic or cretinic deafness kindly presented by Professor F. R. Nager, of Zürich. Fig. 13 shows the deformed stapes adherent to the posterior margin of the oval window and facial canal. There is also well-marked malformation of Corti's organ in all coils and

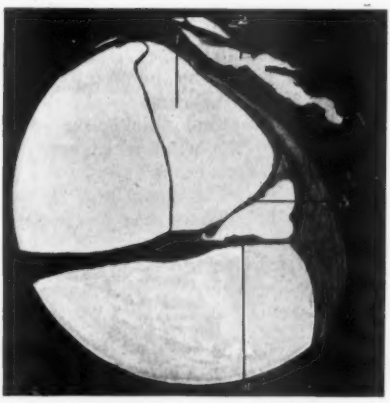

FIG. 5.

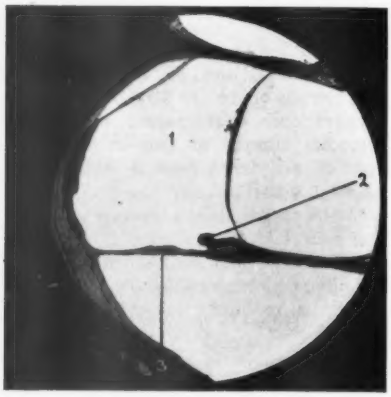

FIG. 6.

FIG. 5.—From a case of congenital deaf-mutism of Scheibe's type. Left ear. Horizontal section through upper part of basal coil, No. 250. × 45 diam. 1, Dilated cochlear duct. 2, Split in the bony capsule (artefact). 3, Adhesion between membrana tectoria and stria vascularis. 4, Rudimentary Corti's organ.

FIG. 6.—From same case as Fig. 5. Horizontal section through lower part of left middle coil, No. 250. × 45 diam. 1, Dilated cochlear duct. 2, Membrana tectoria lying on the apex of the limbus. 3, Rudimentary Corti's organ. 4, Spiral ligament showing dropsical degeneration. The stria vascularis appears to be well formed.

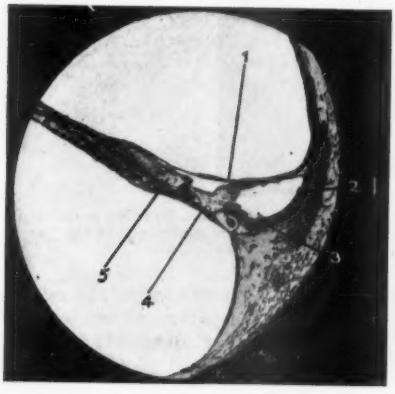

FIG. 7.

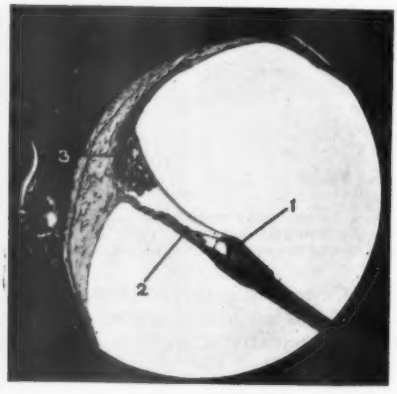

FIG. 8.

FIG. 7.—From same case as Fig. 5. Right ear. Vertical section through upper part of basal coil, No. 55. × 50 diam. 1, Reissner's membrane depressed and attached to deformed Corti's organ. 2, Position of stria vascularis, which is absent. 3, Position of spiral prominence. 4, Basilar membrane. 5, Membrana tectoria tucked into internal spiral sulcus. It will be seen that there is a complete malformation of the epithelium lining the cochlear canal, which is represented by at least four spaces in the section.

FIG. 8.—From same case as Fig. 5. Vertical section through lower part of right middle coil, No. 55. × 50 diam. 1, Membrana tectoria, which lies between the origin of Reissner's membrane and the limbus. 2, Rudimentary Corti's organ. 3, Great proliferation of stria vascularis, which occupies the outer third of the narrow cochlear canal.

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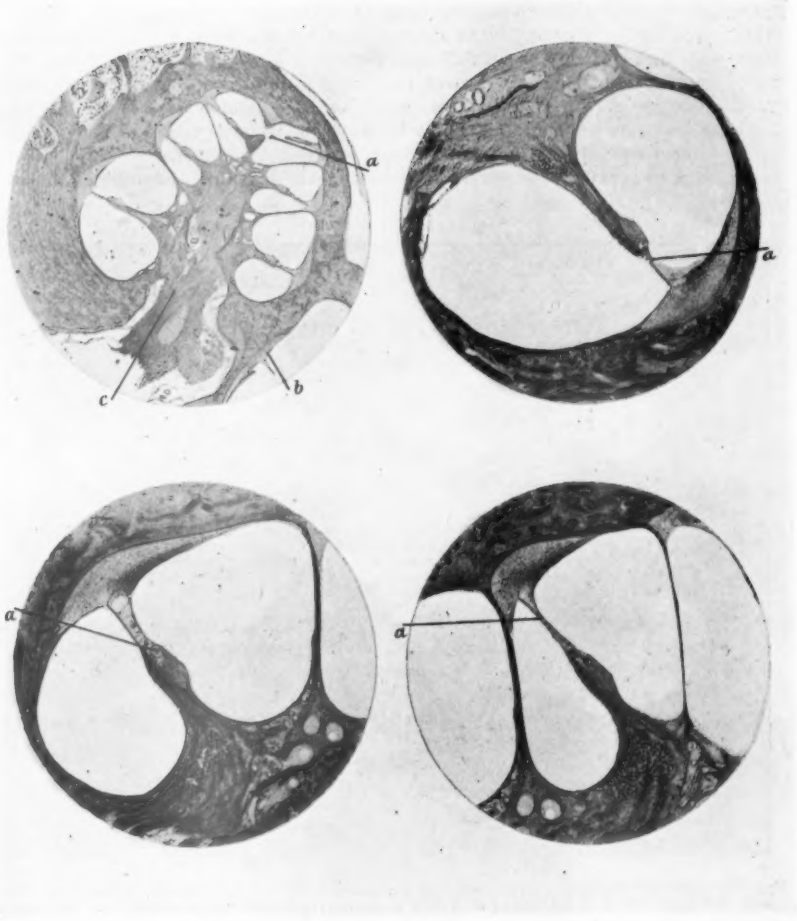

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FIG. 9.—Horizontal axial section through right cochlea of congenitally deaf white bull-terrier pup. Section 120, × 10 diam. Note that the bony capsule and modiolus are normally formed. *a*, Helicotrema; *b*, Collapsed saccule; *c*, Normal cochlear nerve.

FIG. 10.—Horizontal section through lower part of basal coil of right cochlea of same case. Section 150, × 30 diam. *a*, Collapsed cochlear duct. Note that the spiral ganglion and nerve are normal.

FIG. 11.—Horizontal section through upper part of basal coil in same case. Section 150, × 42 diam. *a*, Membrana tectoria tucked into internal spiral sulcus. The cochlear duct is collapsed and Corti's organ malformed.

FIG. 12.—Horizontal section through upper part of middle coil in same case. Section 150, × 45 diam. *a*, Complete collapse of cochlear duct, Reissner's membrane being adherent to the basilar membrane. The membrana tectoria as in Fig. 11. Note well-developed ganglion cells.

absence of the spiral ganglion in the basal coil. Fig. 14 shows deformity of the stapes, hyperostosis of the promontory and marked narrowing of the round window niche which is filled with connective tissue.

(2) *Inflammatory or acquired deaf-mutism.*—(*a*) *Deaf-mutism may be due to trauma*, e.g., fracture of the cranial base involving both labyrinths. About 3% of cases of acquired deaf-mutism are of traumatic origin. Unless the injury to the labyrinth occurs during the first ten years of life, deaf-mutism does not result. Nager's patient was a man, aged 64, who at the age of 4 received a severe head injury. Microscopic examination showed normal middle ears. The labyrinth capsules showed traces of old vertical fracture at right angles to the long axis of the

FIG. 13.—Endemic deafness. Specimen kindly presented by Professor Nager. × 5½ diam. Shows 1, Head and posterior crus of stapes adherent to facial canal and posterior edge of oval window. 2, Facial canal: the nerve is very small.

petrous pyramid. The canals were filled up with new bone and the perilymphatic space of the vestibule greatly reduced by connective tissue and bone formation (fig. 19). The cochlea also showed bone formation (fig. 20) in the perilymph space, great dilatation of the cochlear duct, and degeneration of the neuro-epithelium.

Figs. 15 and 16 are from a case of recent fracture of the base showing fracture of the labyrinth capsule with hæmorrhage into the inner ear. Figs. 17 and 18 are from a second case, showing fracture of the labyrinth with otitis media, labyrinthitis and meningitis. Figs. 19 and 20 are from the above-mentioned case of deaf-mutism due to fracture of the skull in childhood (kindly presented by Professor Nager).

FIG. 14.—Endemic deafness. Specimen kindly presented by Professor Nager. × 6 diam. 1, Deformed stapes in oval window; there is considerable thickening of the submucosa of the oval window niche. 2, Greatly thickened promontory; it is the periosteal bone which is specially involved. 3 and 4, Marked narrowing of niche of round window, which is filled up with connective and fatty tissue.

FIG. 14*a*.—Endemic cretinism. Photograph kindly presented by Professor Nager.

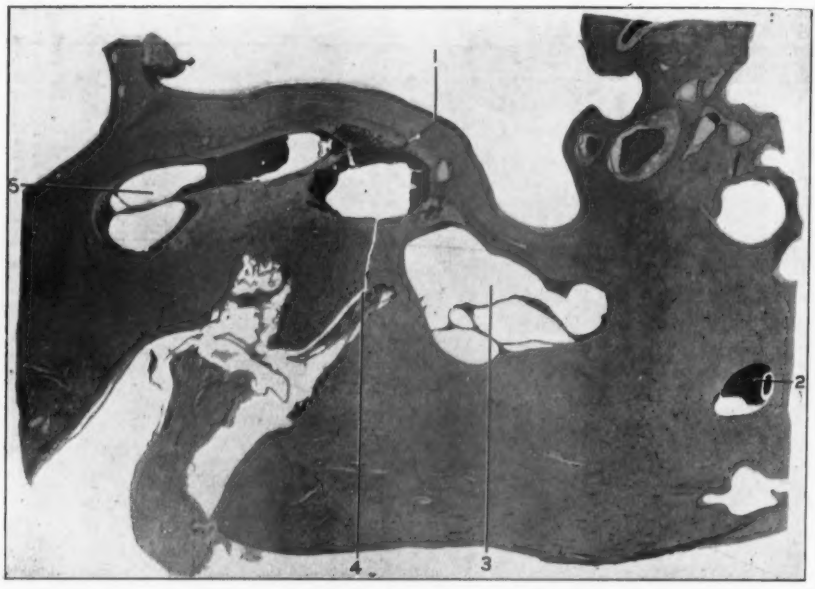

FIG. 15.—Fracture of cranial base with injury to labyrinth capsule. Horizontal section through right ear just above round window, No. 235. 1, Fracture of promontory. 2, Both peri- and endo-lymph spaces of posterior canal contain blood. 3, Vestibule with slight hæmorrhage. 4, Line of fracture reaches canal for nerve to ampulla of posterior semicircular canal. 5, Basal coil of cochlea with hæmorrhage in all three scalæ.

FIG. 16.—From same case as fig. 15. Horizontal section through right ear. No. 78, × 30 diam. 1, Scala media of middle coil, with slight hæmorrhage. 2, Blood in scala vestibuli of basal coil. 3, Rupture of Reissner's membrane. 4, Blood in spinal ligament. 5, Blood below basilar membrane.

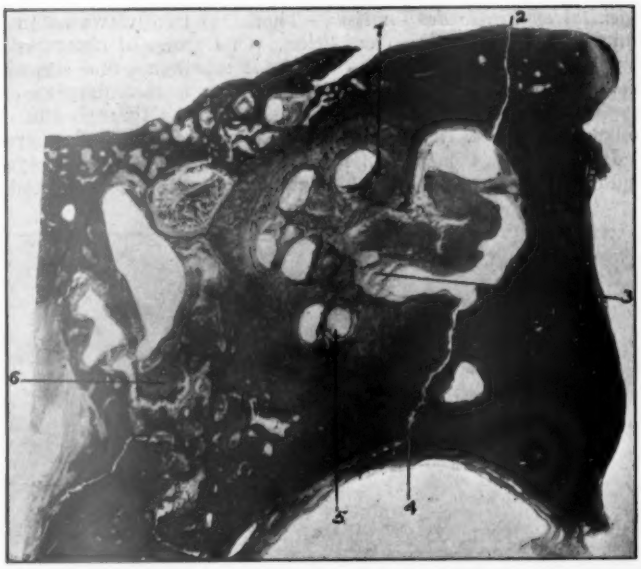

FIG. 17.—From a second case, showing fracture of the labyrinth with otitis media, labyrinthitis and meningitis. 1, Scala tympani of basal coil filled with hæmorrhage. 2, Fracture. 3, Cochlear nerve. 4, Lower end of fracture. 5, Basal coil. 6, Exudate in tubal part of tympanum.

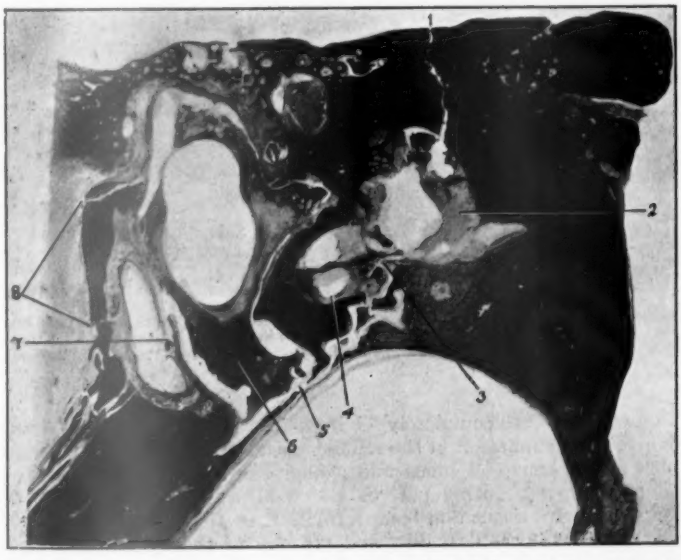

FIG. 18.—From the same case as fig. 17. 1, Fracture. 2, Exudate in vestibule. 3, Fracture of bony spiral lamina. 4, Scala tympani. 5, Fracture of tympanic floor. 6, Exudate in tympanum. 7, Perforation of drumhead. 8, Fracture of meatal wall.

(*b*) *Congenital syphilitic deaf-mutism.*—There are two views as to the nature of the pathological changes in this condition. One group of observers holds that congenital syphilitic deafness is due to syphilitic meningitis and secondary neuro-labyrinthitis. The other view is that the condition is secondary to otitis media which, in syphilitic children, does not clear up but breaks through the windows or invades the bony capsule of the labyrinth and so reaches the hollow spaces of the inner ear. In Gradenigo's case both labyrinth windows were destroyed and the vestibule and cochlea were practically filled up with new formed bone and connective

FIG. 19.—Deaf-mutism due to fracture of skull in childhood. × 6 diam. 1, footplate of stapes. 2, Perilymphatic space of vestibule largely filled up with new-formed bone. 3, Dilated saccule. 4, Cochlea: the basal coil especially shows new-formed bone and connective tissue. 5, Markedly atrophic 8th nerve.

tissue. The canals were completely obliterated. In Schlittler's case there were remains of a past inflammation in the middle ear, as shown by bony ankylosis of the joint between the malleus and incus and spongification of the anterior crus of the stapes and of the neighbouring part of the oval window niche. The inner ear showed new connective tissue and bone formation in the perilymphatic space, with marked dilatation of the cochlear duct and atrophy of the epithelial nerve endings. Schlittler concluded that the condition had been one of genuine primary otitis interna.

Figs. 21, 22 and 23 show the changes in middle and inner ear in a case of the late form of congenital syphilitic deaf-mutism (J. S. F.).

(*c*) *Deaf-mutism due to labyrinthitis following purulent meningitis.*—The original focus of infection may be situated in the nose and paranasal air cavities and the naso-pharynx (especially in epidemic cerebrospinal meningitis), the parotid gland in mumps, the bones in cases following osteomyelitis, the lungs in measles, pneumonia and influenza, or the tonsils in scarlet fever. Probably the next stage is a blood infection as a result of which the organisms are carried to the meninges and set up

FIG. 20.—Deaf-mutism due to fracture of skull in childhood. × 6 diam. 1, Scala tympani of basal coil of cochlea entirely filled up by new bone and connective tissue. 2, Aqueduct of cochlea.

purulent meningitis. From the meninges the infection passes to the labyrinth, within the pia arachnoid sheaths of the eighth nerve, or along the aqueduct of the cochlea. In the first stage of neuro-labyrinthitis the hollow spaces of the inner ear are filled with blood-stained serum which later becomes purulent and results in complete destruction of the membranous labyrinth. This is followed by the formation of granulation and connective tissue and finally by new bone formation. The base of the cochlea is more affected than the apex but in some cases the cochlea is completely obliterated.

Meningitis may occur in the fœtus in utero but such a condition is difficult to prove. Cases of deaf-mutism, however, have been recorded in which the patient was apparently deaf from birth and in which microscopic examination of the middle ear showed normal conditions. The appearances present in the labyrinth corresponded to those seen in undoubted cases of meningitic labyrinthitis.

Fig. 24 is from a case of neuro-labyrinthitis due to epidemic cerebrospinal meningitis (J. S. F.). Fig. 25 is from a case of meningitis due to measles and pneumonia (J. S. F.). Fig. 26 is from a case of deaf-mutism following measles and meningitis, kindly presented by Professor Nager.

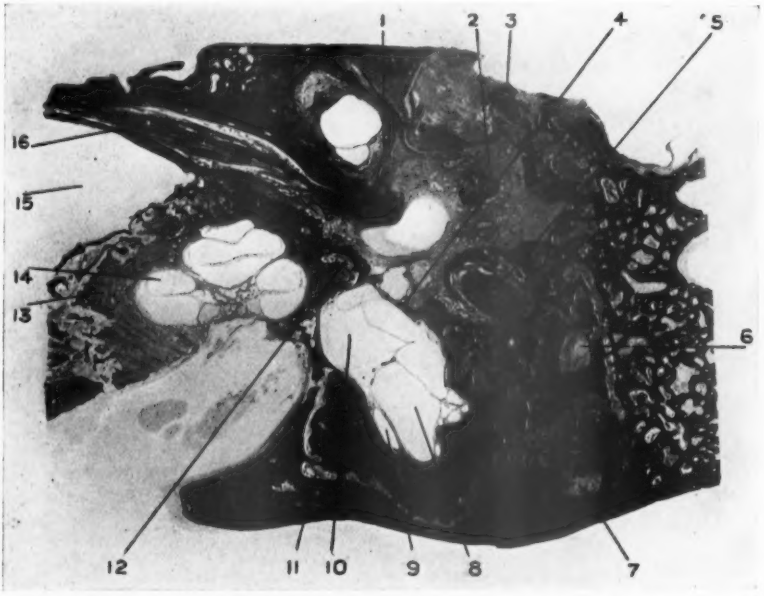

FIG. 21.—Congenital syphilitic disease of the ear. Horizontal section through left ear. No. 282, × 5 diam. 1, Tendon of tensor tympani. 2, Long process of incus. 3, Necrosed bone being extruded into external meatus. 4, Footplate of stapes. 5, Facial nerve. 6, External canal, the perilymph space is filled with granulation tissue. 7, Posterior canal, also filled with granulation tissue. 8, Utricle. 9, Ductus endolymphaticus. 10, Dilated saccule. 11, Osteoclastic marrow, which, higher up, erodes the internal meatus. 12, Osteoclastic marrow in bone of promontory in anterior margin of oval window. 13, Bony capsule of cochlea. 14, Dilated scala media of basal coil of cochlea. 15, Carotid canal. 16, Tensor tympanic muscle. Note the erosion of the bony capsule of the cochlea by the osteoclastic marrow.

(*d*) *Deaf-mutism due to labyrinthitis following middle-ear suppuration.*—Denker states that middle-ear lesions alone do not produce such severe deafness as to give rise to deaf-mutism. If, however, the otitis media invades the labyrinth through the windows on both sides, bilateral labyrinthitis is set up and, if the child is very young, results in deaf-mutism.

Microscopic examination in these cases shows, as a rule, not only evidence of middle-ear suppuration but also closure of the round window niche by new formed bone. Here again the changes in the basal part of the cochlea are more marked than in the apical coil. The vestibule usually shows dilatation of the utricle and saccule,

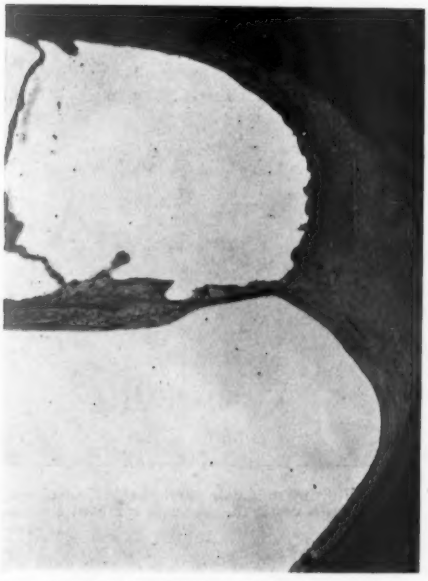

FIG. 22.—From same case as fig. 21. Left ear. Section 320, × 50 diam. Shows condition (degenerative neuritis) of Corti's organ in basal coil.

FIG. 23.—From same case as fig. 21. Left ear. Section 340, × 210 diam. (Kulschitzky stain.) 1, Vein in modiolus. 2, Spiral ganglion of basal coil, showing *atrophy of nerve cells*.

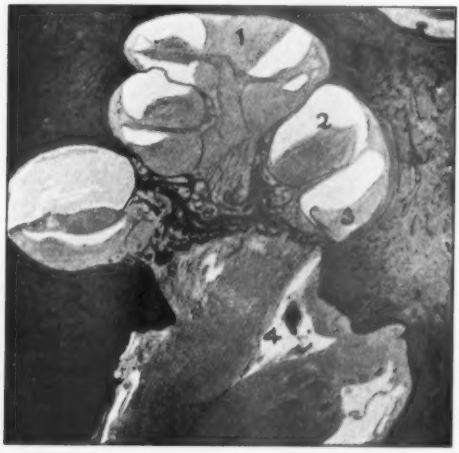

FIG. 24.—Neuro-labyrinthitis following epidemic cerebro-spinal meningitis. × 9 diam. 1, Helicotrema with purulent exudate. 2, Scala vestibuli. 3, Scala tympani containing pus. 4, 8th nerve in internal meatus surrounded by pus.

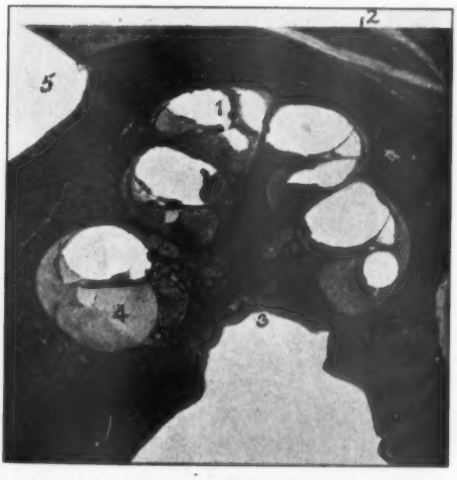

FIG. 25.—Neuro-labyrinthitis following measles and pneumonia. × 9 diam. 1, Helicotrema with purulent exudate. 2, Tensor tympani. 3, Fundus of internal acoustic meatus with pus (the nerve was unfortunately pulled out post-mortem). 4, Scala tympani of basal coil containing sero-purulent exudate. 5, Carotid canal.

with connective tissue and bone formation in the perilymph space. The canals are often obliterated.

Alexander Mercer (case not previously recorded). The patient was first brought to the Royal Infirmary, Edinburgh, in 1910, at the age of 16 months. Examination

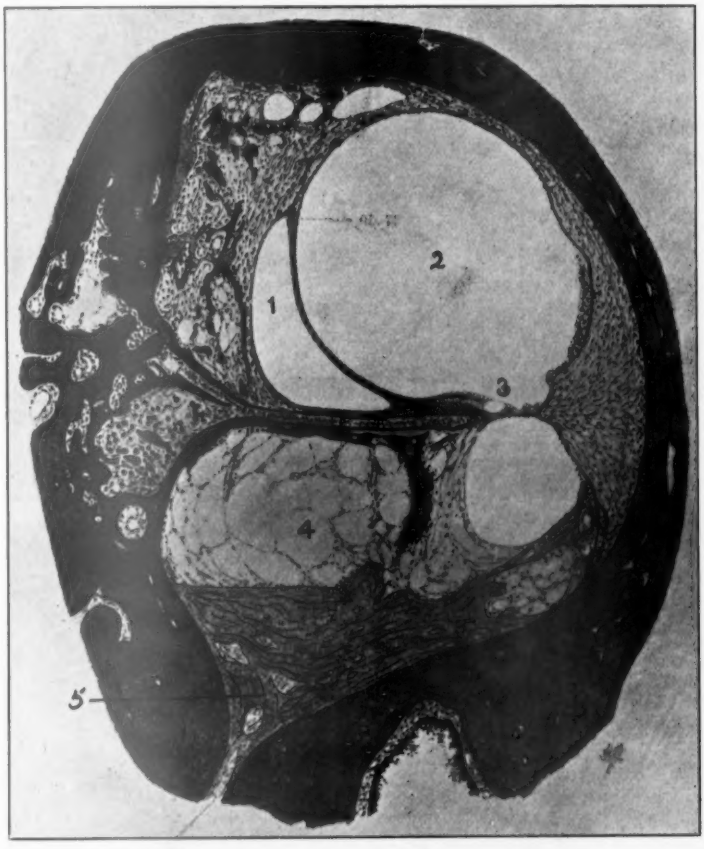

FIG. 26.—Professor Nager's case of deaf-mutism due to neuro-labyrinthitis following measles and meningitis. 1, Remains of scala vestibuli which has been greatly narrowed by new bone and connective tissue formation and also by dilatation of 2, the cochlear canal. 3, Atrophic Corti's organ. 4, Scala tympani filled with connective tissue. 5, Cochlear opening of perilymphatic aqueduct filled up by new bone formation.

showed bilateral purulent otitis media. Enlarged tonsils and adenoids were removed. Six months later the radical mastoid operation was performed *on both ears* at another hospital. The patient was brought back to the Royal Infirmary in August, 1923; at that time he was being educated at Donaldson's Hospital as a deaf-mute. The

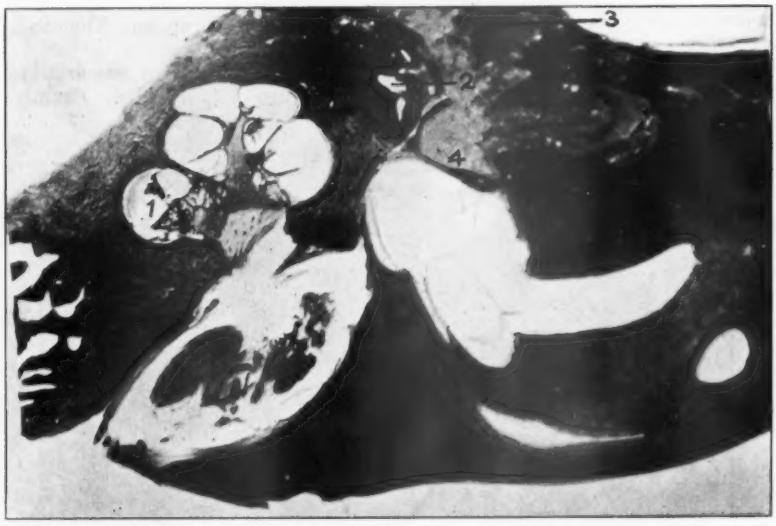

FIG. 27.—Deaf-mutism following purulent otitis media and labyrinthitis. Right ear: horizontal section 120. × 6 diam. 1, Basal coil of cochlea showing new bone formation. 2, Spongification of anterior margin of oval window. 3, Connective tissue in tympanic cavity: note that the radical mastoid operation had been performed. 4, Footplate of stapes.

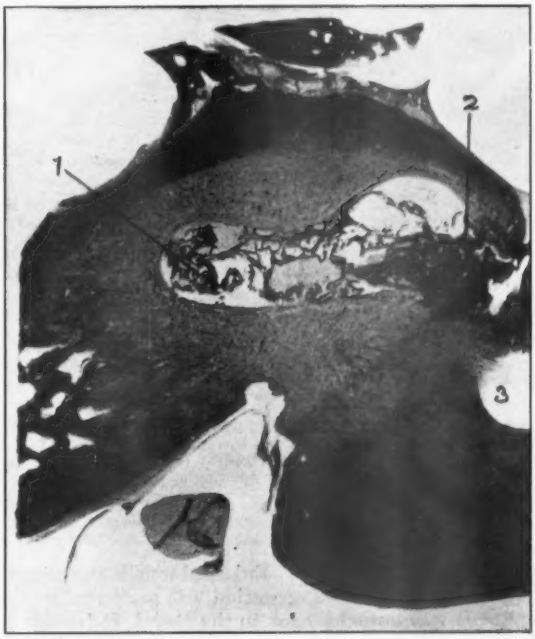

FIG. 28.—Right ear: horizontal section 193. × 6 diam. 1, Upper part of basal coil of cochlea filled with new bone. 2, Scala tympani and round window niche obliterated by new bone formation. 3, Ampulla of posterior vertical canal, normal.

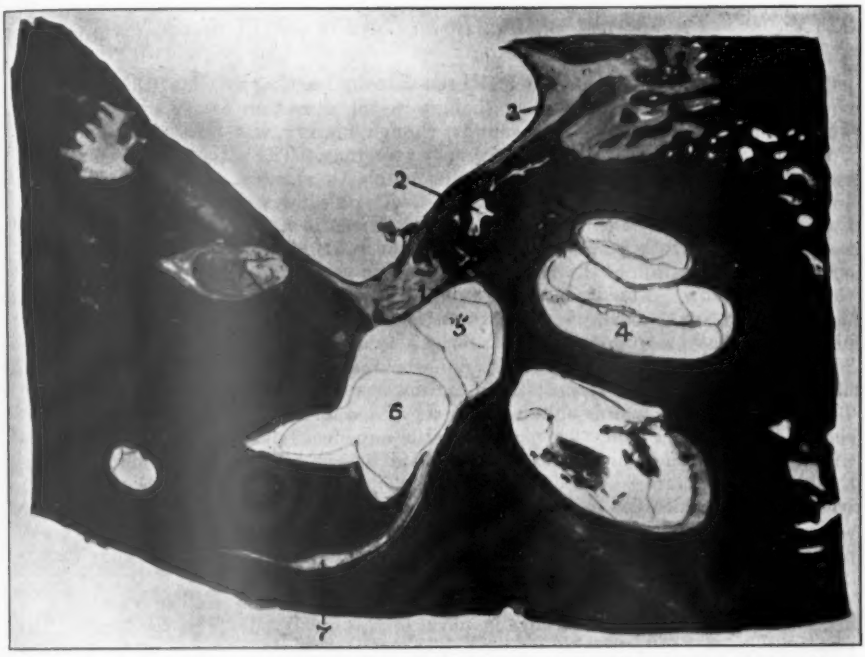

FIG. 29.—Left ear: horizontal section 279 (× 6½ diam) showing 1, Footplate of stapes. 2, Spongification of labyrinth capsule in anterior margin of oval window. 3, Squamous epithelium lining radical mastoid operation cavity. 4, Cochlea: the scala media is dilated but Corti's organ is fairly well formed. 5, Dilated saccule. 6, Dilated utricle. 7, Aqueduct of vestibule.

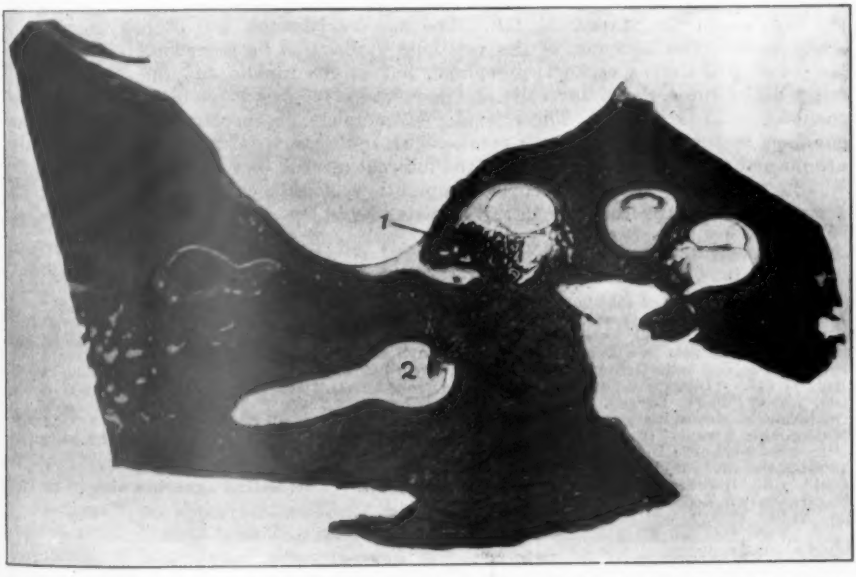

FIG. 30.—Left ear: horizontal section 353 through basal coil of cochlea. × 6 diam. 1, Scala tympani in region of round window filled up by new bone formation. 2, Ampulla of posterior vertical canal, normal.

patient's parents stated that he had been late in learning to walk. Examination showed masses of desquamated epithelium in the operation cavity on both sides. The boy appeared to hear loud sounds, though his cry was that of a deaf child. Cold syringing of each ear produced prompt nystagmus. The patient died in a medical ward in December, 1929, aged 21 years, from aplastic anæmia.

Microscopic examination of the right ear.—The medial wall of the middle ear is lined by squamous epithelium. Beneath this there is a thick layer of connective tissue, and below this again there is erosion of the periosteal bone. There is considerable dilatation of the Haversian spaces in the bone of the anterior margin of the oval window. The Eustachian tube is closed by connective tissue (radical mastoid operation). There is a break in the bony canal of the facial nerve and the nerve itself has protruded through this gap (possibly result of operation) (fig. 27). The crura of the stapes are absent, and the niche of the oval window is largely filled up with connective tissue: there is, however, no bony ankylosis of the stapes. The round window niche is obliterated by new bone formation (fig. 28), and the basal coil of the cochlea and the perilymphatic aqueduct show a similar condition. (Apparently the infection of the scala tympani in the basal coil had burst through the basilar membrane and cochlear canal and involved the scala vestibuli.) Elsewhere in the cochlea the scala media is greatly dilated, practically obliterating the scala vestibuli. The spiral ganglion cells are degenerated, especially in the lower coil, and there is here a considerable amount of small cell infiltration. Corti's organ is degenerated in all coils.

The neuro-epithelium of the utricle is healthy, but the otolith membrane is detached (artefact ?). The saccule is more or less collapsed. The aqueduct of the vestibule appears to be normal. The membranous semicircular canals and cristæ are healthy (figs. 27 and 28).

Microscopic examination of the left middle and inner ear shows somewhat similar conditions. The round window niche is filled up by new bone (fig. 30). The saccule is dilated and its membranous wall is in contact with the medial surface of the footplate of the stapes (fig. 29). The neuro-epithelium and otolith membrane are present. The aqueduct of the vestibule appears to be somewhat dilated. In the basal coil Corti's organ is atrophied, but in the middle and upper coils it is fairly well formed, the pillar cells and membrana tectoria being clearly seen. The cochlear canal is dilated. There is almost complete degeneration of the cochlear ganglion in the basal coil, with small-celled infiltration. The utricle and canals are normal, as are also the nerves in the internal meatus (figs. 29 and 30).

(In regard to the microscopic examination of this case, the writer begs to acknowledge a grant from the Moray Research Fund.)

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Towards the Prevention of Deaf-Mutism: A Review of Forty Years' Progress.

By J. Kerr Love, M.D., LL.D.

It is not often that an observer is privileged to compare the figures attached to his own work after so long a period as forty years. It is over forty years since I began work at the Glasgow Institution for the Deaf and Dumb, now known as the Langside School for the Deaf, and it is with the figures collected at that school, and from other Scottish schools, that I have chiefly to deal with in the first place. For the most part I shall avoid census returns, because these are not given in the details necessary, nor are they reliable enough for the purpose of this meeting. The earlier figures were gathered as the result of a circular letter which I addressed to all British schools in 1895 after four years' work at the institution. The later figures were collected for me by Mr. Haycock in response to a similar appeal in 1931.

In 1891 the population of Scotland was about	4,000,000
In 1931 ,, ,, ,, ,, ,, about	4,800,000
In 1895 the deaf in Scottish Schools were ...	524
In 1931 ,, ,, ,, ,, ,, ,, ...	534

This is nearly 17% of increase of population with a practically stationary number of deaf children in schools and this in spite of an increasingly severe combing of the population by school-attendance officers for cases of deaf-mutism. Corrected for the increase of population, there should have been 100 more deaf-mutes in 1931 over the number in 1895. The ratio of acquired congenital cases was, in 1895, as nearly as could be ascertained, 50%. I cannot go into the details of this calculation here, but the basis of it is fully given in my book on "Deaf-Mutism" published in 1895 (McLehose, Glasgow).

The ratio in 1931 was: Congenital, 72·2; acquired, 27·8.

Population of Scotland	1891 ...	4,025,647
,, ,, ,,	1931 ...	4,800,000
Deaf in Scottish schools	1895 ...	524
,, ,, ,, ,,	1931 ...	534
Ratio of acquired cases	1895 ...	50%
,, ,, congenital ,,	1895 ...	50%
Percentage of acquired cases	1931	27·8
,, ,, congenital ,,	1931	72·2
Average family in deaf cases	1895	5·5
,, ,, ,, ,, ,,	1931	4·0

Ratio of deaf born in congenital families = 3·30, which is as near the Mendelian ratio as one could expect in such small numbers.

The average family in congenital cases was in 1895, 5·5 children; in 1931, 4 children. This decrease can hardly be accidental. It is perhaps due to a deliberate effort to reduce families by birth control, an effort which we can hardly condemn in families with hereditary deafness. The decrease has occurred too in spite of the greatly lowered infantile mortality rate since 1895. The ratio of deaf born to hearing in congenital families is 1 to 3·3 which is as near the Mendelian ratio as one could expect in dealing with such small numbers. Parents are loath to ascribe deafness in a child to heredity. Were the truth known, I believe the Mendelian ratio would be more nearly correct. The returns are made from schedules filled up by medical officers, but even there the medical officer has seldom been the observer of the illness causing deafness.

Comment on these figures might be made to spread over the whole field. I shall content myself with one or two features. The most striking feature is the diminution of the ratio of adventitious or acquired cases, a fall of nearly 26%—from 50 to 27·8%. And this has taken place in the face of an increasingly severe

combing of the schools for backward cases of all kinds. What has caused this good result? The answer is: chiefly medical inspection and treatment. Teachers are instructed to refer backward cases to medical officers. Treatment is at once instituted and is continued by skilled nurses over a longer period (a period of at least ten years) than in any other Institution.

I can hardly avoid mentioning in this connection the operation for the removal of tonsils and post-nasal adenoids. It may surprise some of you too—even those of you who are busy with this operation—that 25% of the youth of this country are without tonsils and post-nasal adenoids.

We admit to the schools in Glasgow 22,500 children annually, and in school hospitals, general and special hospitals we remove in at least 6,000 children tonsils and post-nasal adenoids.

The better housing, better feeding and better clothing of school children are all contributing to the diminution of acquired deafness, as also the greater cleanliness, especially of the hair and head of children at school. Lastly the treatment of the ear complications of scarlet fever and measles to a finish in the case of children in hospitals for infectious diseases This movement has been under way for too short a time for its full effect to be estimated, but I am sure it will later show its effect in the lessening of acquired deaf-mutism. But a link is still awanting in the chain of treatment. It is not always possible to arrest the suppuration in these cases before the patient is dismissed. The result is gradually increasing deafness, danger to the life of the child—for it is nearly always a school child—and sometimes the carrying of infection from the hospital to children outside, because the discharge from scarlet fever ears remains infectious occasionally for months. What is the awanting link? On conversation on this subject, I presented the difficulty to Dr. Arbuckle Brown of the Glasgow Education Authority, and he made the following suggestion: "That all children taken into hospital suffering from any disease (infectious or other) wherever any indication of ear complication has been discovered during the illness, should be kept under observation for as long as may be necessary and if need be attended to at one of our school clinics for observation or treatment. Cases which have developed otorrhœa, even when the case has been "cured" and the child discharged with a dry ear, whether in hospital for the usual period or for an extended period, are to be dealt with in a similar manner, namely, by attending an observing clinic for an extended period to ensure that there is no return of the discharge. If treatment is necessary then the child will attend a treatment clinic. The chronic cases in which disease of the mastoid cells has occurred will be dealt with by admission to a hospital for operation." That I think is a necessary step in the treatment of the school child, and this system is now in operation in the City of Glasgow.

Syphilis is a cause of both congenital and acquired deaf-mutism. My complaint against this disease is not only that it causes deafness—and this it does both in children and adults—but that it ruins families. In a series of family trees which I collected and published in 1912 the following figures came out: In 21 families there were 172 children involved, there were 30 stillborn children, including these there were 75 deaths of children nearly all in the first and second years, and in addition there were 31 deaf or deaf and blind children. Of the remaining 66 children few survived to adult life.

Are we dealing with success in preventing this disease? We are not, and the reasons are that we have no compulsory notification and we cannot compel treatment. Here is the state of matters in the City of Glasgow (Medical Officer's Report, 1929):

"Even with all the facilities for treatment, the individuals suffering from venereal disease do not take advantage of the treatment to a cure. The voluntary system does not seem to be a success." In Dr. MacGregor's latest report just

quoted, the percentage of defaulters before completion of treatment is stated to have been 55·3% in 1923 and 77·1% in 1929. The average percentage in default during the past five years was 70·5%.

There seems nothing for this disease but compulsory notification and compulsory treatment to a finish in every case. Only thus will the hearing and the lives of such deaf children be saved. The objection to compulsory notification of all cases of primary disease is that this would induce the sufferer to conceal the condition. I do not think this objection could be urged against the compulsory notification of the disease in children, a step which I urged on the Royal Commission on venereal diseases many years ago. No parent would see his child die or become deaf because he preferred to hide the condition from which the child suffered. And the power to compel treatment to a finish should be given by Parliament now. The waste of time and money incurred by incomplete treatment is a sufficient reason for compelling the continuance of treatment to a finish. I here make a public appeal for the notification of venereal diseases in children, and I do so not only in the interests of the deaf child but of the families of syphilitic parents. Lastly, let me say a word on hereditary deafness. Whilst a great deal has been done for the prevention of acquired deafness nothing has been done or is being done for the prevention of hereditary deafness except by voluntary birth control by the deaf themselves. Were this effort confined to the deaf one would say: "Just let it go on." But it is being carried out even to a greater degree by the hearing, and particularly by the better classes amongst the hearing. One cannot look at the thousands of small bungalows growing up all over this country without misgiving. I call these "birth-control houses." They are built to accommodate only one child or, if there is a second baby, it is an Austin. But the average family in hereditary deaf cases is four.

Why should we not educate the deaf children in our schools—say during their leaving year, which is the sixteenth of their lives—on the principles of Mendelism and its bearing on the unions most of them are bound to make? Most of the hereditary deafness we have would diminish rapidly were this instruction given and followed. But would it be followed? you ask. Well, till the instruction is given we have no need to give an answer. Ours is to tell the deaf the truth.

Conclusions regarding the further prevention of deaf-mutism—So much has been done for the prevention of acquired deafness during the forty years of my review that my chief feeling is one of profound thankfulness. In addition to the continuance of present preventive measures I suggest the following:—

(*a*) The linking up of the school authority with the infectious diseases hospitals for the control and cure of all the ear complications of the infectious diseases.

(*b*) The compulsory notification of all cases of venereal disease as soon as possible and the immediate notification of all cases of deafness or of any other defect or condition due to venereal disease when such appears in a child.

(*c*) The teaching of sex physiology by way of lessons in Mendelism to all deaf children and their parents or other relatives, during the last year of the school life of the child.

(*d*) The encouragement of birth-control in families in which hereditary deafness exists.

Discussion.—Mr. F. BRAYSHAW GILHESPY (Birmingham): Excepting those who are consultants at institutions for the deaf, otologists have little chance of contact with those responsible for the education of our deaf population. Probably in the past we might have given the teachers of the deaf more help but have failed to do so owing to lack of knowledge of their requirements. It is important, on receiving a deaf-mute for instruction, to know what remains of hearing, if any, are present. Ewing, of Manchester, a notable teacher of the deaf, had certain deaf-mutes referred to him who, when they made any attempts at speech or sound, did so with normal intonation—not in the lifeless intonation of the totally deaf.

Owing to the different diagnoses expressed as to the auditory acuity, by various otologists, Ewing was forced to rely on his own investigations to get at a satisfactory measure of their deafness. It was my duty to review his book "Aphasia in Children," which contained an account of these investigations and, briefly, I would like to bring this work to your notice in order to draw your attention to the work going on in these institutions for the deaf.

The most interesting portion of this book refers to a study of seven children, who, when brought to the author for speech training, were aphasic, on account of deafness, either congenital or acquired soon after birth.

The history of one of these patients is typical of the other six, and illustrates Ewing's thesis. In March, 1924, a boy, aged 4½ years, was seen by him. Up to the age of 3 years he had given no signs of being able to hear. Later, when he was examined by otologists, there was thought to be some hearing present, as his pupils dilated when a tuning fork was sounded close to his ear. At the age of 4½ years be behaved, on the whole, like a congenitally deaf child; he could not understand a word said to him and could not speak. He expressed his wants by "cries" which were not words, but at the same time there was normal intonation of the voice in these cries, unusual in any prelinguistic form of deafness. Unlike the born-deaf child, he did not slur his feet when walking and he was neat in his movements. Apparently it was found impossible to test him by tuning forks, although I am not entirely convinced of this. Ewing developed a tunnel-test used in conjunction with an audiometer. This is extremely ingenious, as the child depresses the switch when he hears the note of the audiometer, but thinks that it is the noise of the train which is set going through the tunnel at the same moment.

Ewing found, after testing this group of children, that their hearing for 64, 128, 256 d.v. fell definitely within the distribution for children of normal hearing but that there was a severe defect for hearing of the higher frequencies. He called this "high-frequency deafness." This term to me now indicates nerve-deafness, but it has a great hold amongst those responsible for teaching the deaf and is bound, sooner or later, to be brought to the notice of otologists. That is one of my reasons for bringing Ewing's work to your notice.

Various workers have shown that vowel sounds have special frequencies, which lie between 375 d.v. to 2,400 d.v., while the consonants have frequencies higher up the scale, mostly in the region of 8,000 d.v. a second. Therefore, a child with nerve-deafness would not hear consonants but might appreciate vowel sounds. The following table, taken from Harvey Fletcher's "Speech and Hearing," shows further that the vowels have two frequencies,

Characteristic Frequency of the Vowel Sounds.

Speech sound	Low frequency	High frequency
ū (pool)	400	800
u (put)	475	1,000
ō (tone)	500	850
a (talk)	600	950
o (ton)	700	1,150
äh (father)	825	1,200
a (tap)	750	1,800
e (ten)	550	1,900
er (pert)	500	1,500
ā (tape)	550	2,100
i (tip)	450	2,200
ē (team)	375	2,400

sometimes widely apart. Inability to hear a tuning fork above 1,000 d.v. would account for the difficulty in distinguishing two vowels, supposing their lower vibration period was the same, but one of the vowels also had a vibration period higher in the scale than 1,000.

I have a patient who demonstrates clearly this point of difficulty. He can discriminate $\overline{AH}$ and $\overline{OO}$ with the left ear, up to nine feet, but gives $\overline{OO}$ for $\overline{EE}$ even at one inch, except when a loud voice is used, and then not with certainty. The right ear confuses $\overline{OO}$ for $\overline{EE}$ however close one gets. This is explained by the fact that $\overline{EE}$ has two characteristic frequencies widely apart, one at 375 d.v. and one at 2,400 d.v. A normal child would distinguish $\overline{EE}$ from $\overline{OO}$, which have very similar lower frequencies at 375 d.v. and 400 d.v. by the higher frequency at 2,400 d.v., characteristic of $\overline{EE}$. If the child cannot bear 2,400 d.v. clearly, then he will be unable to distinguish $\overline{EE}$ and $\overline{OO}$ as the lower frequency of $\overline{EE}$ is very near that of $\overline{OO}$.

When it is seen that the vowels go in pairs and that the second of each pair sounds to the deaf child exactly like the first of the pair, it will be realized what confusion may arise in a child's mind on account of the vowels alone. Added to this he fails to hear the consonants. He has been likened to a person listening to the worst loud speaker ever heard. He lives in a world of nonsensical sound, for "I'll be back soon," he might hear "OO BOO BAW OON."

Being conversant with all the arguments against the use of the Western Electric Audiometer and knowing that Ewing, in his research, had not the opportunity of testing bone-conduction, I have carefully tested my patient with tuning fork and audiometer, and I think that there can be no doubt that his is a case of nerve-deafness, with hearing for the lower part of the scale and that the explanation for the phenomenon shown, as offered by Ewing, is correct. In testing deaf people I have not found the islands of hearing referred to by Kerr Love in his early work. A chart drawn up by Shambaugh suggests that the loss of hearing in certain parts of the scale is a relative, rather than a total, loss.

[I wish here to record my thanks to Mr. Cockersole, of the Birmingham Institute for the Deaf, who first introduced me to this work.]

Mr. A. D. SHARP said that the incidence of deaf-mutism for Europe was given as 8 in 10,000; in Britain, he thought, the figure was about 2 in 10,000. With regard to the proportion of congenital to acquired deaf-mutes, he found the percentage to work cut at 60% congenital and 40% acquired. Of the congenital cases, 34% had no hearing, 66% had remnants of hearing, 3% of whom had evidence of fair hearing, but were unable to comprehend or make use of it.

In 10% of the absolutely deaf congenital cases, deaf-mutism was present in a near relative. In no case of congenital deaf-mutism were the father and mother related. Syphilis did not account for more than a fraction of the cases. In the acquired cases, deafness was noticed after the following illness: pneumonia, meningitis, acute otitis media, measles, scarlet fever, whooping cough, teething, diphtheria and trauma.

While birth control by those who have a family history of deaf-mutism will reduce the number of congenital cases, there is not likely to be any real diminution in the number of acquired.

Sir JAMES DUNDAS-GRANT said that to read about deaf-mutism was depressing, but when the subject was put before one by Dr. Love and Mr. Fraser it became invested with new life.

Reference had been made to "deaf-mutism" without deafness. Professor Giampietro many years ago described a number of cases in which the child could not learn to speak but hearing was still present. Obviously there was in that case some defect in the speech centres and special education of these was required.

Walker Downie had described a post-mortem examination in a case of congenital syphilis in which the disease was originally in the meninges, from which it had extended.

In a paper on the pathology of deafness occurring in tabetic paresis, Krasznig stated that the site of origin seemed to be the internal auditory meatus in the arachnoid sheath, where, apparently, there was a constriction behind which the spirochætes could accumulate and from where an extension into the internal ear took place.

Some time ago he saw a case of Schilder's disease with various paralyses attributed to "aphasia." He understood that one of the first symptoms of this disease might be bilateral nerve-deafness, adding another to the difficulties of diagnosis.

The round window was very important for hearing, but only for the high-pitched tones. He, Sir James, had brought forward the case of a woman who had sclerosis of one ear, in which he was able to produce a permanent perforation in the membrane. In her case the round window was plainly visible, and she could hear very high-pitched tones.

Dr. K. B. AIKMAN said the problem of deaf-mutism must be dealt with from a very broad standpoint. The Wood Committee on Mental Defect had shown that the lowest 10% of the population formed a "Problem Group" in which was concentrated a very great deal of physical and mental weakness.

In tackling this "problem group" we struck at foci of zymotic disease which contributed so largely to deaf-mutism, as well as to other sequelæ, and we also struck at many carriers of congenital deaf-mutism; for carriers were often the subjects of other defects, not always deafness. Opinions as to the legality of sterilization were conflicting. A Bill to legalize voluntary sterilization of mental defectives was lately before Parliament and would be re-introduced shortly.

Sterilization of mental defectives would pave the way for voluntary sterilization in other conditions. This would be an advantage to the community and to the deaf-mutes themselves.

Dr. KERR LOVE (in reply) said he considered that congenitally deaf children had an island of hearing somewhere. Any defect there might be in a family was emphasized when cousins married. That was the objection to cousin marriages. With regard to sterilization, the British Medical Association had declared that to be illegal.

The number of cases of acquired deafness had been reduced by 25% since 1895, and he thought the conditions under which cerebrospinal fever was induced would be improved. Forty years hence there would be less congenital deafness, but there were even now more institutions for deaf children in this country than there were deaf children to fill them. The deaf-mute ratio in Scotland and England was diminishing.

Mr. J. S. FRASER (in reply) said that if a child aged 10 years became totally deaf he probably would not become a complete deaf-mute; he would be a "semi-mute."

In regard to the education of deaf children, he did not know whether members of the Section were able to understand the speech of deaf-mutes who had been taught by the oral method; their teachers and mothers could understand them, but he (the speaker) could not.

With regard to congenital cases, he agreed with Dr. Kerr Love that in many of them the patients had some degree of hearing; there were probably little areas of the cochlea which, though malformed, were able to appreciate sound. In acquired cases due to labyrinthitis, however, the whole inner ear was usually destroyed.

He did not enter into the question of brain changes. The French school said that many cases of deaf-mutism were due to changes in the brain. He thought that this was because French otologists had not cut microscopic sections of the inner ear in cases of deaf-mutism; otherwise they would have found it unnecessary to postulate changes in the brain. The celloidin method was laborious, and therefore more suitable to the Teutonic than to the Latin temperament.

From this last case the question arose whether the round window or the oval window was the more important for hearing. The stapes was not fixed on either side, though the oval window was filled up with connective tissue, but the round window on both sides was obliterated by new bone. On the left side, Corti's organ, in the middle and upper coils at any rate, was fairly well formed. Recently Professor Gustav Alexander of Vienna had said that tones from 16 up to 90 d.v. were heard through the oval window, and that tones from 90 d.v. upwards, i.e., the area concerned in hearing speech, were appreciated through the round window. To some extent at any rate, therefore, this last case tended to support Professor Alexander's view. It was at least doubtful whether complete fixation of the stapes would produce such severe deafness as to result in deaf-mutism, but complete bony obliteration of the round window did so.

Mr. GILHESPY, in reply, said that the deaf child heard such an amount of nonsensical noise that he became confused concerning everything, and that was what teachers had to fight against.

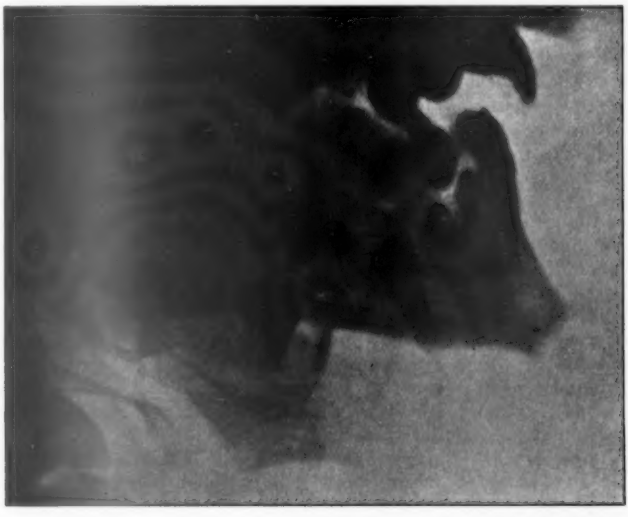
Section of Odontology.

President—Mr. E. B. Dowsett, D.S.O., L.R.C.P., M.R.C.S., L.D.S.E.

[*January* 25, 1932.]

A Case of Spontaneous Fracture of the Mandible.—J. Edgley Curnock, L.R.C.P., M.R.C.S., L.D.S.

This is a case of a spontaneous fracture of the mandible, associated with an acute osteomyelitis of the jaw. There is also some evidence of a pre-existing pathological condition—such as a cyst or a myeloma—of the region. As spontaneous fractures of the mandible are not often seen, I thought this report might be interesting. The patient is now aged 26. During 1930 she noticed a gradual swelling of the right side of the mandible, and in November, 1930, she consulted a dentist, who extracted the first and second molars. The swelling, however, continued to increase in size. In April, 1931, I admitted her into the West London Hospital as she had a rigor and a temperature of 102° F. There was complete trismus and the right side of the jaw was very swollen and tender. On attempting to force the mouth open slightly, it became obvious that there was a



April, 1931

Spontaneous fracture of the mandible following acute osteomyelitis.

fracture in the second molar region and the patient had noticed this herself the previous day. I operated that evening and removed the remaining mandibular teeth on the right side, as they were all extremely loose. An incision was made in the mouth, and the buried wisdom tooth and the second molar root, together with all the pieces of loose bone, were removed. A quantity of soft reddish-brown material was also removed and the pathological report on a section of this stated that it was suggestive of a septic myeloma. I also opened the swelling externally and inserted a couple of drainage tubes. Microscopical examination of the pus showed the presence of hæmolytic streptococci and *Streptococcus viridans*. On the fifth day after the operation a gland in the neck suppurated and the pus from this seemed sterile, but after a fortnight's prolonged incubation a few colonies of *Streptococcus viridans* were grown. The patient has now very good union although there is some deformity.

[*February* 22, 1932.]

The Surgical Treatment of Pyorrhœa Alveolaris.

By H. H. Stones, M.D., Ch.B., B.D.S.

Abstract.—(1) The technique of eradicating the pockets and occasionally trimming the alveolar margin is described. (2) Instruments designed for the operation are illustrated. (3) The whole mouth can be treated at one sitting. (4) The flap operation, in which the gum is reflected before scraping the alveolus and finally sutured, is not advisable. (5) Pyorrhœa can be eradicated by surgical measures in cases favourable for treatment. (6) Recurrence of the disease is due to: (*a*) Lack of suitable preliminary treatment. (*b*) Insufficient attention to detail when performing the operation. (*c*) Lack of suitable post-operative care by dental surgeon or patient. (*d*) Selection of cases not suitable for operation.

Many writers have devoted their attention to the local treatment of pyorrhœa since Riggs [1] considered this aspect of the disease. The procedure of cutting away loose flaps of gum has been advocated at various times. Robitzeck, of Vienna [2], in 1862, was one of the first to adopt this method. G. V. Black [3] referred briefly to the surgical treatment of the pockets in 1915. J. G. Turner [4] in 1923, stated that pockets should be dealt with by excision of the gum-flap, leaving the denuded root accessible to cleaning. E. B. Dowsett [5] in the same year advocated promoting efficient drainage at the necks of the teeth by freely excising the gum to obliterate the pockets, and recently designed a set of scalpels for this purpose. F. St. J. Steadman [6] considers it a useful method in selected cases. L. Widman [7] is apparently one of the first writers to describe a more detailed operation for the treatment of the disease. In his technique he makes a superficial sectional and gingival incision through the mucous membrane only round several teeth. He then dissects this layer, or as he terms it "lambeaux," which apparently chiefly consists of epithelium, away from the underlying granulation tissue, progressing towards the root portion of the teeth until he gets to healthy structures. He now scrapes away this "spongy granulation tissue," exposing the alveolus, all rough projections of which are removed. The procedure is carried out on both buccal and lingual aspects. Finally, the mucous membrane is replaced and the two sides are stitched together. Not more than three teeth are treated at one operation. Treatment on somewhat similar lines has been carried out by other operators [8, 9, 10]. It is strange that though over sixty years have elapsed since operative measures were first recorded, more interest has not been taken in this method. One must infer that the results obtained have been disappointing and that the original condition has recurred. Such a tendency to relapse can be ascribed to various factors, which will be briefly discussed when describing the method of treatment adopted by the writer, but it is necessary to point out the importance of efficient pre-operative and post-operative treatment, of close attention to detail during the operation, and of obtaining the co-operation of the patient. It must be emphasized that surgical treatment should be adopted with discrimination and also that certain measures are essential for success.

(1) The probable ætiology in each particular case must be investigated; and if the causal factor can be discovered, it must be treated before further measures are adopted.

(2) The local condition must be rendered as hygienic as possible.

(3) An autogenous vaccine must be administered.

After these various preliminaries the pockets are cut away.

The operation of gingivectomy.—Anatomically, the aim of the operation is to obliterate the pocket and make the attachment of the gum to the tooth level with

the general surface of the gum, thereby facilitating cleaning, and limiting the risks of stagnation in this area.

The set of instruments designed for this operation consists of four scalpels and two pairs of scissors. They are fashioned in such a way that the pocket, if of operable depth, can be removed wherever it may be situated in the mouth. The scalpels with the curved blades are designed for excising the pocket at the posterior aspect of the last molar tooth. Those with the straight blades are used for the other parts of the mouth. The scissors facilitate the removal of any adherent tags of gum and the trimming of any projecting edges.

The following are the details of the operation:—

Calcium lactate or hæmoplastin is given previously; the bleeding will otherwise probably be copious and impede the operation. Also an injection of atropine $\frac{1}{150}$ gr. is given to lessen salivation. To this is added morphine $\frac{1}{4}$ gr. Latterly, one hour previous to operation, nembutal—one cachet—has been given orally. The part of the gum to be treated is sterilized with iodine, and injected with a solution containing novocain 2%, and adrenalin 1/75,000. The latter, in addition to localizing the effects of the anæsthetic, also restricts the bleeding. For this reason the method of local injection is preferable to nerve blocking by regional anæsthesia.

The following technique is adopted. If the complete mouth is to be treated at one sitting, the operation is performed first on the mandible, otherwise bleeding from the maxilla will ooze over it. One half of it is anæsthetized and operated upon separately, before proceeding to the other half. The maxilla is then dealt with in the same manner. The depth of the pockets and line of incision necessary to obliterate them are estimated from radiographs and by means of a probe. An incision is made on the posterior aspect of the last molar tooth, and is carried round to the buccal surface of this tooth, the incision is carried forward to the anterior part of the same tooth, cutting the gum between it and the adjoining tooth. The incision is continued in a similar manner from tooth to tooth until the incisor teeth are reached.

A similar incision is now made on the lingual aspect of the gum with the curved scalpel, starting at the last molar tooth. It is continued again with the straight edged scalpel to the incisors. Interdentally the incision meets the one already made on the outer side. The excised portion of gum can now be removed. Sometimes both buccal and lingual parts come away in one piece. Frequently they have to be removed separately. Any loose tags of gum left are trimmed down. The cut margins are then treated with the electric cautery, which makes them completely smooth and arrests the hæmorrhage. It is always advisable somewhat to overestimate the depth of the pocket and excise the gum more freely than is apparently necessary. The gum, on both the labial and lingual aspects, must also be cut at an angle to the tooth, not horizontally. Horizontal incision tends to produce excessive granulation tissue, and favours the formation of a fresh pocket. Round one tooth there may be considerably more absorption than round its neighbours, with deeper pocket formation; when cutting away the pocket it is necessary that the incision should be extensive and prolonged to involve the adjoining teeth, otherwise the pocket will re-form. After removing any remaining fragments of seruminal calculus, the mouth is atomized with a mild antiseptic. Finally, all the interdental spaces and exposed surfaces are packed and covered with a suitable material. Sticky wax impregnated with oil of cloves, 1%, and aspirin 5%, has been found to give good results. E. W. Fish suggests a cement made by mixing zinc oxide with oil of cloves. A similar preparation, but using carbolized resin and eugenol, is also recommended by A. W. Ward [9]. Workers abroad advocate curetting any projecting edges of bone; in most cases this has not been found necessary, but where there is a deep interdental pocket, and where the alveolus has been absorbed considerably in this position, it is advisable to round off the alveolus. This is done by reflecting the gum and trimming the bone with a surgical bur or light chisel. On account of the position of the wisdom teeth

it is often impossible to eradicate the surrounding pockets. Under such conditions these should be extracted. It is impressed upon the patient that it is an extensive operation. He is put into a nursing home, if possible for from seven to ten days, to allow of skilled after-treatment of the mouth.

Discussion on other techniques.—It is difficult to see if any advantage can be gained by an elaboration of the method briefly described at the beginning of this paper. The argument in favour of this method is that but little underlying tissue is left exposed uncovered by epithelium. From experiments on dogs suffering from pyorrhœa, where the pockets have been cut away, it has recently been shown in another paper that the epithelium covers the denuded gum in fourteen days. It is also stated that the rarefied alveolus immediately underneath the pocket is usually infected, and for this reason should be curetted. While it is granted that infection may be present, the writer is in agreement with James and Counsell's [11] opinion that this deep infection is a sequela to the gingival inflammation. Hence, it may be reasonably argued that once this source of infection is eliminated, the bone will resume a normal condition. As will be seen, this is substantiated by similar experimental operations on dogs with pyorrhœa. The apparent objection to the flap operation is the difficulty of cutting the gum flap to fit perfectly between the teeth. Any unevenness would predispose to the formation of fresh pockets. In any case the fact of laying fresh pieces of gum between the teeth creates an artificial fresh pocket.

Should it be necessary to operate on the whole mouth, the question has to be decided: whether it shall be done at one time, or on several occasions, leaving an interval between the various operations. Most writers [5, 8], including A. T. Pitts [12], advocate treating several teeth only at one sitting. At first this method was adopted, but it is now the practice after all the preliminary precautions have been taken to complete the whole mouth at one time. The resistance of the patient must, however, be increased against the predominant organism. It is essential to give vaccine treatment first and to continue this until the maximum dose gives no reaction. If this is neglected the operation may produce an intense toxæmia. It has been found that by treating several teeth only at one sitting, and then leaving an interval, the reaction from each treatment was almost as severe as completing the whole mouth in one operation. Pickerill [13] removed all the infected tissue under chloroform. It is difficult to realize how this lengthy operation could be satisfactorily performed under general anæsthesia unless the anæsthesia was unduly prolonged.

It has been suggested that one means of eliminating the pockets is to cut them by diathermy instead of with the scalpel. Until recently the drawback of using this method has been the difficulty of gauging the exact amount of current that should be used.

After-treatment.—The patient is seen daily for a fortnight and the gums are atomized for the first few days with a solution of sodium phenate, which is both antiseptic and analgesic. The general condition of the patients is usually not so serious that they are unable to attend for daily treatment. As soon as the resulting tenderness has subsided the following prescription is substituted:—

℞ Aq. cinnamoni	...	...	½ dr.
Liq. hydrogenii peroxidi		...	2½ oz.
Aquam ad ...	...	...	6 oz.

It is important that all blood-clots should be removed when atomizing the gums, or these clots will suppurate, favouring fresh pocket formation. The patient is instructed to use a mild antiseptic mouth wash, every hour when awake, for the first few days; later it must be used after each meal. Carrel-Dakin solution has been found to give the best results. All applications should be given as cold as

possible. If there is great pain the following prescription is first used as a mouth wash :—

℞ Liquor. potass ... ... 1 oz.
Acid. carbol. glac. ... ... ½ oz.
Glycothymol ... ... 1 oz.
Aquam ad ... ... 8 oz.

Sig.—The mouth wash, one teaspoonful to half tumbler of cool water, to be used after food.

Or the following :—

Aspirin ... ... 10 gr.
Aquam ad ... ... 4 oz.

Sig.—The mouth wash to be used with an equal part of cold water.

The tongue must be cleaned daily.

Sedatives, such as veramon, may be administered orally.

Finally, it is essential that scrupulous attention should thereafter be paid to the hygiene of the mouth, both by patient and dental surgeon, or the condition will return.

The teeth should be scaled at least once every three months, and the patient should be instructed in the correct use of the toothbrush. The teeth should never be scrubbed across the gums, but in a vertical direction only—in the upper jaw downwards, and in the lower jaw upwards. That is, the direction of brushing should be to brush the gums on to the teeth. This prevents any gingival irritation such as will result from incorrect methods. It is noteworthy, after the pockets have been removed, that the amount of seruminal calculus exposed, which has been down in the pockets and overlooked in spite of the most careful scaling, is considerable. The result of the operation is that the teeth appear much longer; if necessary, they can be shortened afterwards by grinding.

Prognosis.—It is obvious that a cure cannot be expected in the generally accepted sense of the word, as this would imply complete restoration of tissues, and no attempt is made by this method to obtain reattachment of the gum and periodontal membrane to the denuded cementum. The aim of the treatment outlined is to eradicate and prevent a recurrence of the disease.

From a consideration of the pathology, bacteriology, and signs of pyorrhœa the following conditions must be fulfilled before the treatment can be considered successful. (1) Clinically, the gums must assume the appearance of those in the normal mouth, and on careful examination with a probe there should be no pocketing. (2) Microscopically, a smear taken from the gum margin should show practically no pus cells.

Bacteriological evidence from the gum margin is also of interest, though the use of it is minimized, as the various organisms found in pyorrhœa are also found in the normal mouth. To test the value of this type of evidence, cultures were taken from the depths of the pockets round certain teeth in a number of cases before treatment. At varying periods of from six to eighteen months after treatment, further smears were taken from the gum margin adjoining the same teeth respectively, and cultivated. The quantity of organisms was considerably reduced in cases showing a good clinical result after treatment. A bacteriological examination of value can be undertaken in those cases in which a streptococcal culture from the alveolar bone itself can be grown [14].

A medium rose-head bur is inserted, under aseptic conditions, through the gum into the alveolar bone, about two millimetres below the crest ; care being taken that the bur does not get warm. After withdrawal, the bur head is inserted into a broth ampoule which is finally planted on various media. A year after treatment another examination should be made, to see if the bone is still infected. As only 17% of human cases examined in this way before treatment have been found to give positive

cultures, at present there is not enough material available to make a definite statement as to whether infected alveolar bone can be rendered healthy. In a recent paper the results of a similar examination of the alveolar bone made on dogs suffering from pyorrhœa were described. Here I found that a positive culture was

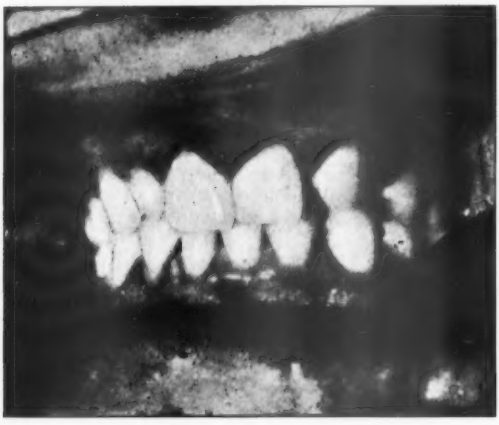


FIG. 1.—Before treatment.

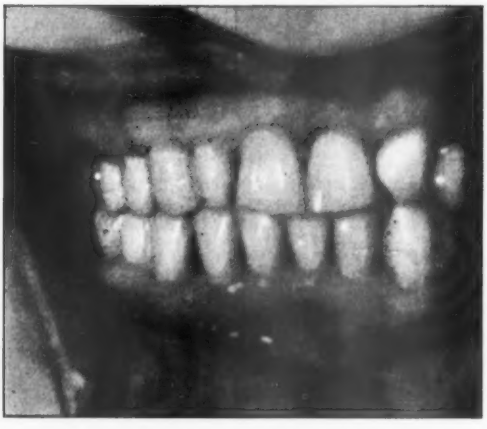
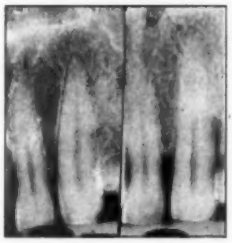


FIG. 2.—One month after.

grown in 62% of cases. Gingivectomy was performed on one side of the jaws and afterwards the dogs were killed at varying periods. Further cultures taken from the same area after operation, proved sterile. In these experiments it was also demonstrated that the histological appearance of the epithelium and underlying tissues of the treated side was more normal.

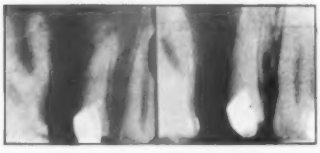
An examination of skiagrams (figs. 3, 4 and 5) taken of cases before and after treatment show that rarefaction is less pronounced, suggesting deposition of fresh bone, and there is formation of a new lamina dura.



(*a*) (*b*)

FIG. 3.

(*a*) Before operation.
(*b*) Fifteen months after operation.



(*a*) (*b*)

FIG. 4.

(*a*) Before operation.
(*b*) Fifteen months after operation.

(*a*) (*b*)

FIG. 5.

(*a*) Before operation.
(*b*) Eighteen months after operation.

The prospect of obtaining a cure is good in those cases that are suitable for treatment. Figs. 1—5 illustrate the condition of cases before and after treatment. In those cases which are not favourable for treatment, and particularly in those in which the cause of the disease cannot be removed, even if the pyorrhœa has not progressed far, the hope of a cure is remote.

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Discussion.—Mr. F. W. BRODERICK said he considered that Dr. Stone's operation was a severe one. He himself had obtained excellent results by destroying the pockets by diathermy. Relapses did not occur in these cases if general medical treatment was instituted with the idea of removing the tendency to the alkalosis which he (Mr. Broderick) believed to be the fundamental ætiological factor in pyorrhœa.

Mr. ARTHUR BULLEID said he thought that, as a preliminary method of treatment, vaccination would be useful but he was not in favour of vaccine administration as a rule in pyorrhœa cases which were being treated on less rigorous lines. There was no doubt that direct smears were a very useful criterion of the effect of treatment, as the smears very often showed that the improvement was less marked than would be expected from the clinical appearances.

A Case of Proliferation of Bone in the Maxilla and Mandible.

By H. H. KENSHOLE, L.R.C.P., M.R.C.S., L.D.S.

FREDERICK C. H. J., aged 70 years. First attended Guy's Hospital, December 9, 1931, complaining of a foul discharge from the left jaw, noticed for some months. Upon visual examination the canine fossæ were seen to be somewhat protuberant, giving, to a certain extent, an appearance of leontiasis ossea, while inside the mouth there was a marked degree of expansion of the alveolar ridges in the maxillary molar and premolar regions, which were edentulous except for the first upper left premolar. Elsewhere there were evidences of proliferation of alveolar bone, such as one sees frequently in connection with chronic infection of the jaws, and which is labelled sclerosing osteitis. Radiographic examination showed the presence of the following roots of teeth $\frac{6\ 4}{}\ |\ \frac{}{5}$ and marked loss of alveolus in the $\frac{3}{}\ |$ region. By pressure upon the cheek, pus could be expressed from a sinus connected with a premolar root, buried immediately beneath the surface. The condition then present was as seen in the model. Under nitrous oxide the three

roots were removed, and an incision was made in the buccal sulcus in the region of the second premolar root elicited the fact that there was a definite recess above the proliferated bone. The first premolar was removed on account of extreme mobility.

On January 18, 1932.—Under endotracheal anæsthesia the mucous membrane over the thickened ridges was reflected, the incisions on both sides being made along the external borders of the masses, so that the final suture lines were not on the ridges, but well up in the buccal sulci. The region thus laid bare was seen to have a smooth ivorine surface of cortical bone, and to be divided into lobules, while fibrous septa stretched from the deep surface of the mucous membrane into the interstices thus made. By circular saws and copper discs, cuts through the bone were made, and passed through quite thin pedicles, allowing the removal of the lateral mushroom-like outgrowths of alveolar bone. The bases of the pedicles having been smoothed, the redundant mucous membrane of the lateral flaps was removed, and the wounds were sutured.

The term "alveolar bone" has been used. It is presumed that owing to chronic infection the normal absorption of alveolar bone has not occurred, rather has there been a proliferation and sclerosis of the alveolus.

It may be contended that the irritation has given rise to neoplastic osteomatous growth, as would seem probable from the pedunculated state. It will be seen that a similar condition of osseous overgrowth is present to a lesser degree in the mandible.

Loss of Calcium Salts from the Dentine of a Dog, associated with Abnormality of the Parathyroids.

By E. W. Fish, M.D.

This case is reported in order to record a loss of calcium salts from the dentine of 15% of the total calcium content of the tissue. The loss was of the nature of a chemical decalcification, there was no "absorption" of the dentine. The dog presented a complicated pathological picture but there is no conclusive evidence of the cause of the derangement in the calcium metabolism. Such particulars as are available of a second case are also reported. The cases were both referred to the author by L. P. Pugh, who regarded them as showing a profound disturbance of the calcium metabolism of a type hitherto unrecorded. No previous instance of a loss of lime salts from the dentine appears to have been recorded though the author has previously shown that calcium salts can be deposited in the fully formed dentine.[1] The analyses were carried out by W. S. Ferguson by a method previously recorded[2] and controlled for accuracy to an error of ± 0·02% of calcium estimated as calcium oxide.

Analyses of the dentine.— Specimens of dentine from two teeth of each dog were analysed and the results tabulated:

		Percentage of CaO.			Average percentage of Ca Oxide.
	Dog A. Spec. 1. ...	30·44	...	...	30·08
	,, 2. ...	29·72			
	Dog B. Spec. 1. ...	33·01	...	...	32·91
	,, 2. ...	32·80			
Normal Control.	Dog C. Spec. 1. ...	35·00			
,, ,,	,, 2. ...	35·08			
,, ,,	Dog D. Spec. 1. ...	34·23			
,, ,,	,, 2. ...	35·37	...	...	35·35
,, ,,	Dog E. Spec. 1. ...	35·79			
,, ,,	,, 2. ...	35·90			
,, ,,	Dog F.	35·76			
,, ,,	Dog G.	35·68			
	Percentage of calcium salts lost in Dog A ...	14·93			
	,, ,, ,, ,, ,, ,, Dog B ...	6·76			

Post-mortem findings.—Dog A (male). The bones were elastic and easily bent by hand pressure. The lower jaw and the roots of the teeth could be cut with a sharp knife. A skiagram of the skull together with that of a normal dog is shown (figs. 1 and 2). The mouth showed acute ulcerative stomatitis. The heart and arteries showed chronic endarteritis, and the kidneys, chronic nephritis. The prostate was enlarged to several times its normal size. The parathyroids were also enlarged to several times their normal size and were fibrotic, showing cellular degeneration and abnormal distribution of the cellular elements. A photomicrograph is appended together with a control from a normal dog. The thyroid, adrenals and other ductless glands were normal. There was a large peritoneal cyst. The age of the dog was approximately nine years. It was killed when it became obvious that it could not get better.

1 Fish, E. W., *Proceedings*, 1926, xix (Sect. Odontology 59-72).
2 *Ibid.*

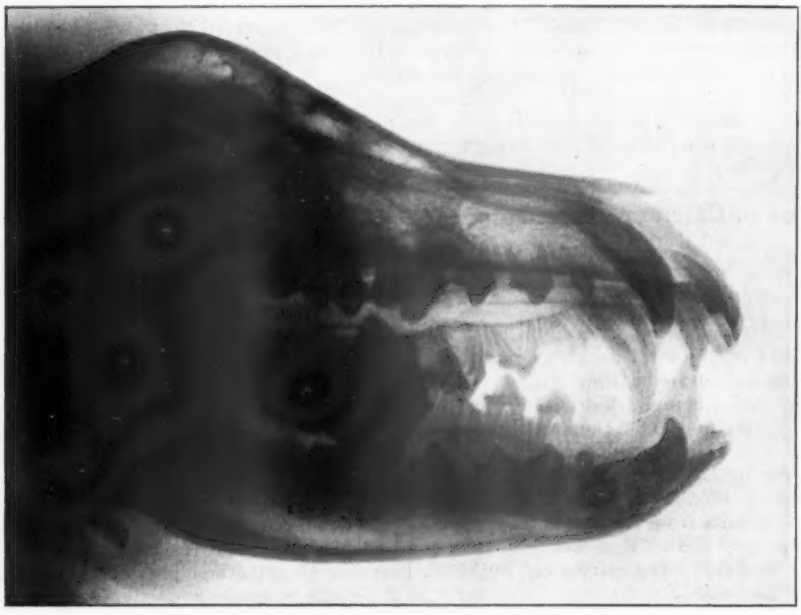


FIG. 1.—Skiagram of skull of normal dog.

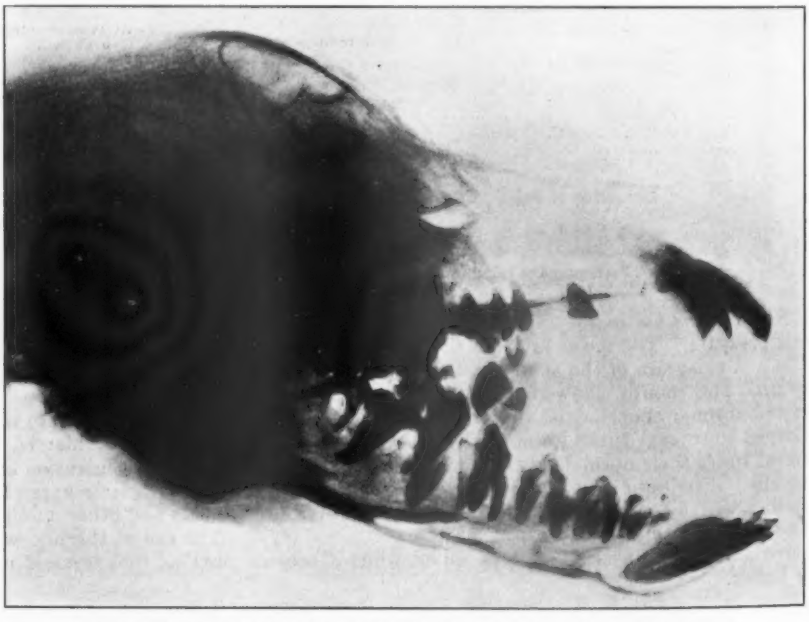


FIG. 2.—Skiagram of skull of Dog A showing loss of calcium salts from the bones

Dog B.—Only the teeth and jaws were available, and these were not so soft as in Dog A. Major Pugh reports that there were nephritis and acute ulcerative stomatitis in this dog also, and that it was an old animal.

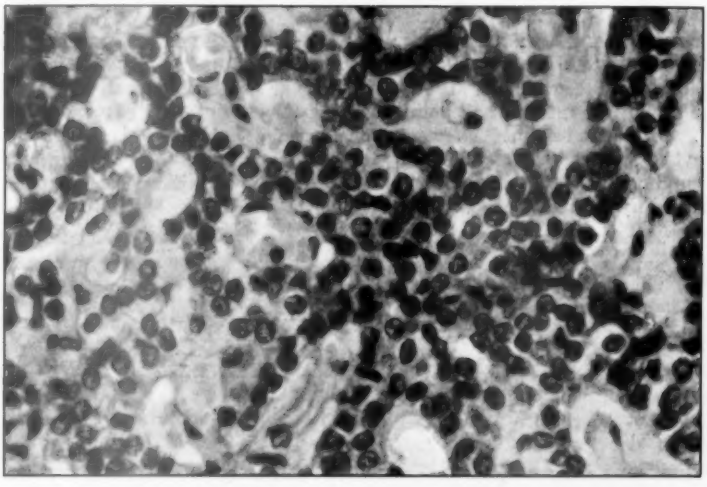


FIG. 3.—Photomicrograph of normal dog's parathyroid.

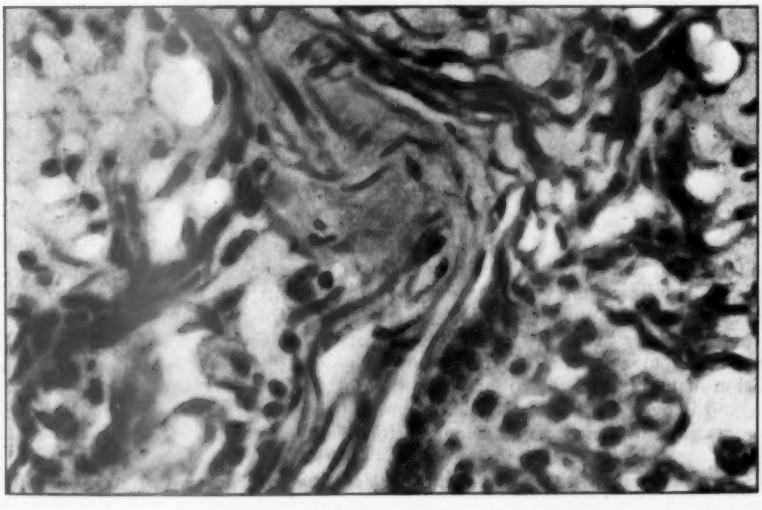
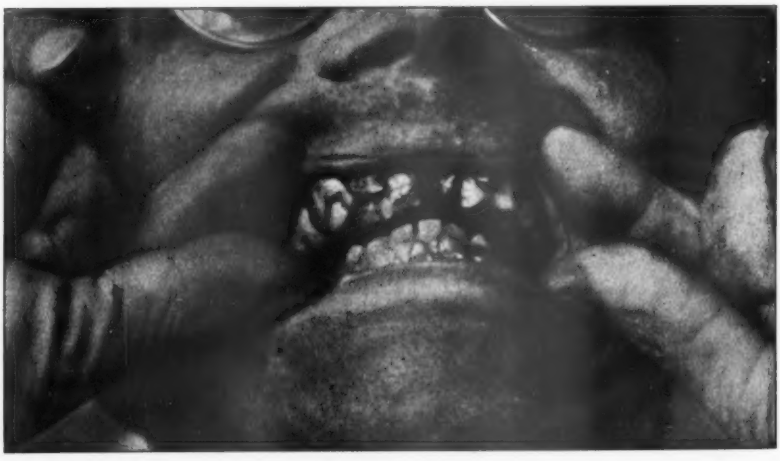


FIG. 4.—Photomicrograph of parathyroid of Dog A, showing cellular degeneration, fibrotic changes and altered distribution of the cellular elements.

Observations.—These cases indicate that it is possible for the dentine to be robbed of its calcium under certain circumstances. The degeneration of the parathyroids may be significant in the case of Dog A. The close agreement of the

analytical findings for the two specimens from a given dog suggests that there was a true disturbance of the calcium metabolism, and that analysing the dentine might serve as a valuable method of controlling experiments on the calcium metabolism of dogs.

Scorbutic Gums in an Adult.—F. PARKES WEBER, M.D. (introduced by P. LLOYD WILLIAMS, M.R.C.S.).—The patient, a pale man, aged 39, was admitted to hospital on February 20, 1932, with turgid "spongy" gums and follicular petechiæ on both legs. He had pain in the legs, which almost prevented him from walking. A blood-count showed considerable anæmia:—Hæmoglobin 42%; erythrocytes 2,260,000; colour-index 0·93; leucocytes 5,200 (polymorphonuclears 66%; lymphocytes 24%; monocytes 10%); the red cells showed some anisocytosis, but hardly any poikilocytosis; the thrombocyte-count was 340,000. His diet for



Scorbutic Gums.

many years had been calculated to produce experimental scurvy, but the symptoms of scurvy had arisen only during the last two weeks: spongy gums, purpura (chiefly of the hair follicles on the legs), and pains in the legs. Two years ago he had had temporary purpura, which disappeared without hospital treatment. The pain and purpura in his legs are already much better (February 22) under simple antiscorbutic measures. At the hospital recently I saw a somewhat similar condition of spongy scorbutic gums in a slightly rachitic infant, cutting its incisor teeth, and it was the pain in the legs which helped me to the diagnosis of scurvy. The gums soon became normal under ordinary anti-scorbutic measures.

Postscript (March 23, 1932).—The patient rapidly improved. On March 21, before leaving the hospital, a blood-count gave: hæmoglobin 86%; erythrocytes 4,800,000. The scorbutic swelling of his gums had subsided, but some pyorrhœa alveolaris remained. It should be added that there was no gastric achlorhydria in this case and that the Wassermann reaction was negative.

Section of Tropical Diseases and Parasitology.

President—Professor J. GORDON THOMSON, M.B.

[*January* 7, 1932.]

Synthetic Anti-Malarial Preparations.

A Discussion of the Various Steps which led to the Synthesis and Discovery of "Plasmoquine," and a Brief Account of its Use in Tropical Medicine.

By Professor Dr. W. SCHULEMANN,

Elberfeld, Germany.

WHEN my colleagues and I took up the problem of the synthesis of anti-malarial preparations in the Bayer-Meister-Lucius Research Laboratories, we had solid foundations to build upon—foundations laid piece by piece during several decades by other workers.

In 1880 Laveran discovered the malarial parasite, and in 1891 Grassi and Feletti found in birds a parasite similar to that of human malaria. In 1895, Ross, stimulated and directed by Manson, discovered the rôle played by the mosquito in transmitting the disease.

How bird malaria might be used for the study of malarial treatment in man was investigated by Kopanaris and the brothers Sergent, but it was not till 1924 that a satisfactory technique was evolved by our colleague Dr. Roehl, whose recent early death we most deeply regret.

Roehl worked out a method of using canaries for experiments on lines closely approaching the conditions of practical therapy, so that it was possible to try out and assess in the laboratory many groups of drugs. This method was fully described by Roehl himself in Düsseldorf in 1926. Wagner Jauregg began the treatment of general paralysis by artificially infecting the patient with malarial parasites. This led Colonel S. P. James to introduce natural inoculation through the mosquito, and so to formulate a method by which clinical and therapeutic tests of anti-malarial drugs could be carried out on the human subject even in this northern climate.

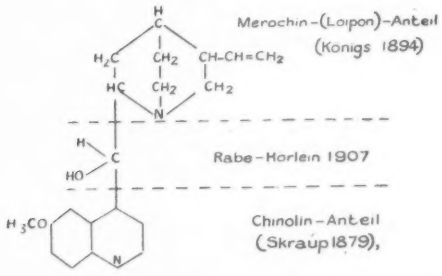
The therapeutic action of chinchona bark in malaria was recognized by the natives of Peru centuries ago, and in 1638 the physician de Vega used the bark to treat the wife of the Spanish ambassador, the Countess of Chinchon, who was suffering from malaria, so that its properties became known in Europe.

In 1820 Pelletier and Caventou prepared quinine from the chinchona bark, and the work of many investigators during the next half century finally enabled its chemical constitution to be formulated.

Diagram I shows the formula which is now ascribed to quinine.

Attached to a quinoline ring, which was identified by Skraup in 1879, there is a basic heterocyclic group (meroquin or loipon group), which Königs described

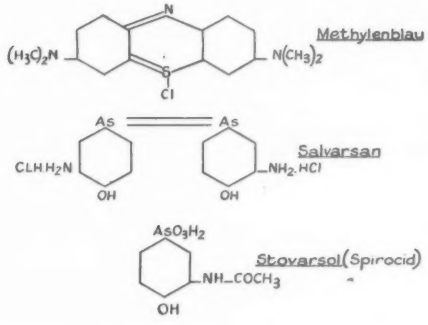
DIAGRAM I.



in 1894. These two parts are united by a bond. On a suggestion from Hörlein, this formula, now generally accepted, was laid down by Rabe in 1907.

An extensive series of experiments was undertaken with the object of discovering other combinations which might be effective in malaria, but the only ones with any definite action were found to be methylene blue and salvarsan. The constitution of these is shown in Diagram II.

DIAGRAM II.



Ehrlich and Guttmann discovered the action of methylene blue in 1891, and Werner, in 1910, that of salvarsan.

Later, Marchoux tested the anti-malarial action of stovarsol (spirocid), a drug prepared by Fourneau from an intermediary product of salvarsan.

In connection with the constitution of quinine, an extensive series of synthetic products was prepared by many investigators with a view to finding an effective compound against malaria. It was generally assumed that an anti-malarial drug must contain a quinoline nucleus, with an aliphatic basic group bound by a carbon bond to the fourth position of quinoline. In spite of much excellent synthesis, however, the desired goal was not reached.

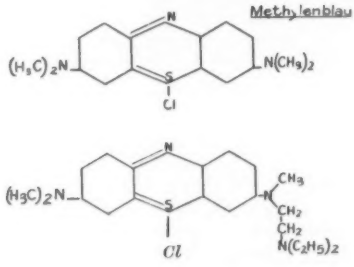
My two colleagues Schönhöfer and Wingler, together with myself, based our experiments on methylene blue. In one of the aromatic amino groups of methylene

blue we substituted an aliphatic basic group in place of an alkyl radical (one of the methyl groups).

This is shown on Diagram III.

Roehl found this compound to be effective in bird malaria, but it had the definitive characteristics of a dye-stuff. Therefore we transferred the experience we had gained from methylene blue to the quinoline group. Contrary to the earlier views of other authors, we did not unite the basic aliphatic radical by a carbon bond

DIAGRAM III.

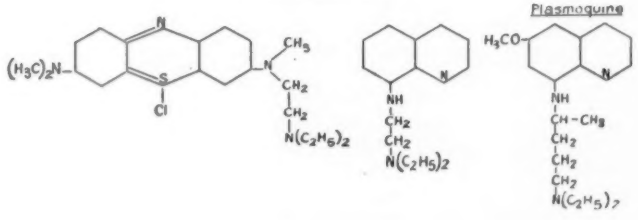


in the fourth position, but with a nitrogen bond to the quinoline nucleus. The first compound of this series which we prepared was a derivative of eight (8)—amino-quinoline. Roehl found this to have a marked therapeutic action on proteosoma infections in canaries. The hydrochloride of this compound had a yellow colour, but without the properties of a dye.

Diagram IV shows the formula.

This new knowledge formed the basis for further work, and by full and free collaboration between chemists and physicians these beginnings were developed.

DIAGRAM IV.



We changed the position of the amino groups in the quinoline ring, introduced every conceivable substitute in the quinoline nucleus in addition to the amino group, and also used many other heterocyclic rings. Furthermore, we varied the side chains and finally the basic aliphatic group.

Diagram V shows a few examples of variations of the side chains.

The length of the carbon chains was altered, and it was made into branched chains in many different ways. We interrupted these chains with single or multiple ethereal oxygen and sulphur atoms and intermediate amino groups. We introduced free or esterified hydroxyl groups into the carbon chains and made many further variations.

The action of all these compounds was tested in animal experiments by Roehl, and from among them we chose plasmoquine for practical clinical investigation.

DIAGRAM V.

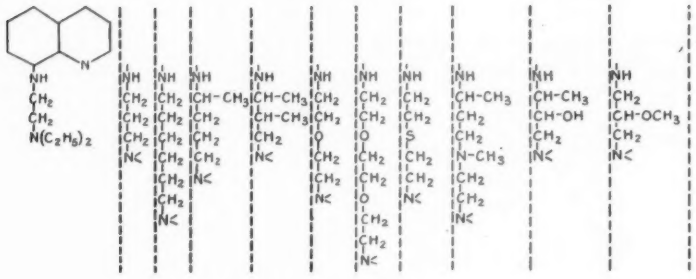
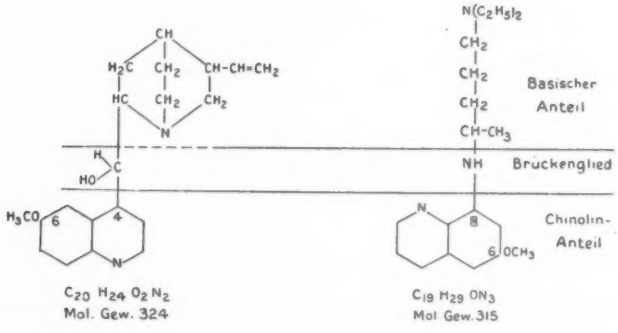


Diagram VI will enable you to compare the constitutional formulæ of quinine and plasmoquine, and to make the comparison clearer the quinoline ring in the plasmoquine formula is placed upside down.

The basis of quinine, as of plasmoquine, is six (6) methoxy-quinoline. In quinine there is a carbon bond in the fourth position, while in plasmoquine an amino group is the bond in the eighth position. In both quinine and plasmoquine the attached side chain is a basic aliphatic residue. In quinine this residue is a tertiary amine, in which the aliphatic nitrogen is joined in a heterocyclic ring. The basic fraction of plasmoquine contains a tertiary nitrogen without a ring. A further interesting fact is that the gross formula and the molecular weights of both compounds differ very little.

DIAGRAM VI.



On the basis of the toxicological and chemo-therapeutic properties we selected plasmoquine in 1925. Sioli found it therapeutically effective in malaria artificially inoculated for general paralysis.

In naturally acquired human malaria the action of plasmoquine was demonstrated by Roehl, who was also the first to discover that plasmoquine destroyed the gametocytes of *Plasmodium falciparum* within a few days, a result which cannot be achieved by quinine. This was a surprising fact; it meant that our work had not

produced a substitute for quinine. Plasmoquine is a synthetic anti-malarial drug, but in its therapeutic properties it differs from quinine.

The first clinical experiments with plasmoquine on a large scale were carried out by Mühlens and his co-workers, by Manson-Bahr and many others. Following this pioneer work, and with the assistance of many investigators, the development of plasmoquine therapy proceeded apace.

But I neither wish to detail here a bibliography of all the papers which have been published on plasmoquine, nor, on the other hand, do I intend to speak about the therapeutic value of plasmoquine in malaria. I propose to deal in this paper only with those facts which, in my opinion, are of importance in indicating the lines of further investigation.

It is to-day well established that the three types of *Plasmodium*, *Plasmodium vivax*, *Plasmodium malariæ* and *Plasmodium falciparum*, react to drugs in a definitely different way, although the reactions are not fundamentally different.

We know, for example, that arsenic compounds have a distinct therapeutic action on *Plasmodium vivax*, but they have, on the other hand, little effect on *Plasmodium falciparum*. Again, *Plasmodium malariæ* is influenced therapeutically to a certain extent by methylene blue, while on *Plasmodium vivax* this effect is small and on *Plasmodium falciparum* it is non-existent. Quinine does not produce the same effect on all three species; it is most potent on the parasites of benign tertian malaria, less active on those of quartan, and least of all on those of subtertian malaria. This is particularly the case in acute malarial attacks.

With regard to relapses, particularly delayed relapses, quinine has less effect on *Plasmodium vivax* than on *Plasmodium falciparum*, that is to say, the relapse-rate following quinine therapy is considerably higher in tertian malaria than in subtertian malaria. These variations in the action of quinine against different types of *Plasmodium* would indicate that the various stages of development of the parasites react to drugs in different ways.

The investigations carried out with plasmoquine confirmed this. The work of medical officers in British India, among whom I would particularly mention Sinton, Knowles, Wallace and Manifold, demonstrated that with plasmoquine therapy, or with plasmoquine combined with quinine, it was possible to reduce the relapse-rate of tertian malaria from fifty (50) per cent. (the usual rate associated with quinine administration) to between two and five per cent. (2-5%).

In subtertian malaria the results do not appear to have been quite so satisfactory, although here also there seems to have been a certain reduction in the number of relapses following plasmoquine therapy.

On the other hand, extremely interesting results were obtained in subtertian malaria with regard to the action of plasmoquine on the gametocytes. Observations on this action have, however, not established any definite facts so far. All we can definitely assert is that in regard to *Plasmodium vivax* plasmoquine acts on the schizonts as well as on the gametocytes. We cannot as yet form a definite opinion on the action of plasmoquine on the gametocytes of tertian malaria, and we await with interest the outcome of the investigations of the Institute in Kuala Lumpur, in the hands of Kingsbury and Amies.

At the moment it is only in subtertian malaria that we can assess plasmoquine with any degree of accuracy. Quinine acts effectively on the schizonts of *Plasmodium falciparum* and allays the acute clinical symptoms, but it cannot inhibit the development of gametocytes—in fact, it appears to stimulate this phase. Plasmoquine, on the contrary, has practically no effect on the subtertian schizonts, but it definitely does destroy gametocytes in a few days. The early view that plasmoquine could inhibit the formation of gametocytes has not been confirmed. On the other hand, the work of Barber, Komp and Newman, Withmore, Roberts and Jantzen, in the hospitals under the direction of Deeks of the United Fruit

Company in Central America, definitely proved that even minimal doses of plasmoquine which were too small to cause the subtertian gametocytes to disappear, sufficed nevertheless to render the gametocytes incapable of infecting the anopheles.

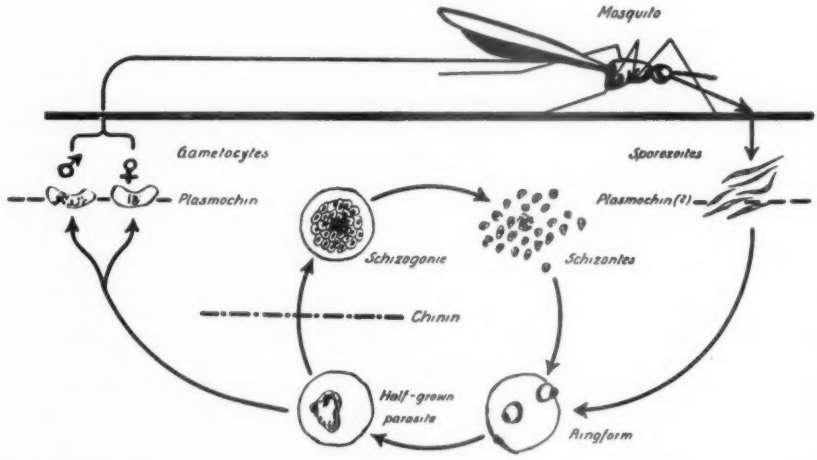
Here, then, for the first time, it appeared possible effectively to break the cycle of infection—man—mosquito—man. Naturally, this gave rise to the consideration of malaria prevention by means of plasmoquine administration—where experience in former years had shown that quinine alone was not sufficient. If it were possible to prevent the anopheles from becoming infected by giving a drug to the human host, then, in theory at least, malaria might be stamped out.

Barber wrote to me recently to say that in West Africa he had succeeded in putting these theoretical conclusions into practice. He intends to publish his results in the near future.

In practice, however, one must never lose sight of the fact that it will be possible only in exceptional cases to treat the population of a malarial district so thoroughly and regularly by means of drugs that every gametocyte-carrier can be included, and so render it impossible for any mosquito to become infected. I am in entire agreement with Sir Malcolm Watson that the discovery of plasmoquine has in no way rendered superfluous the usual sanitation methods directed towards the extermination of the mosquito. At the same time the advent of plasmoquine will provide a new and important weapon allied with sanitation in the fight against malaria.

In considering the places of development of the malaria parasite as I have portrayed them in diagram VII—and I confine myself here purposely to subtertian

DIAGRAM VII.



Subtertian Malaria

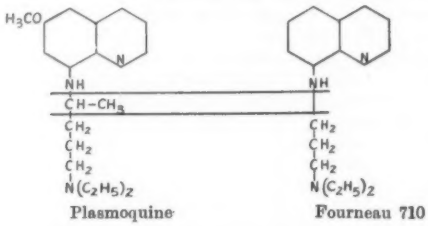
malaria—we see first, a half-grown parasite arising from the schizont. This parasite can continue its development in two directions—the growing parasite can either turn to schizogony, against which quinine is active and plasmoquine inactive, or else gametocytes may be formed, against which plasmoquine alone is effective while quinine is not. As I have set out already, we can assume with certainty, in

subtertian malaria, that quinine breaks the cycle of development at the · — · — · — · — · line, while the point of attack of plasmoquine is marked in — — — —

There are however two points in this scheme of development which have hitherto escaped attention. The first is that we know neither which phase of the parasite gives rise to relapses or recurrences, nor what drug affects this phase.

A second point is the question whether there is a drug that affects the phase of development occurring between the sporozoite inoculated into the human body by the mosquito, and the ring form. If so, what drug? It is to this problem that Warrington, York and Macfie have turned their attention; they showed that in transmitting malaria from one general paralytic patient to another through the medium of mosquitoes it was not possible to obtain a prophylactic action with quinine, even when administered in maximal daily doses. Thus these observers were able to show that quinine has no causal prophylactic action in malaria. Thus quinine suppresses the symptoms of infection, but does not prevent infection. The latest work of James shows that plasmoquine on the other hand in doses of 0·06 gramme daily for six days acts as a causal prophylactic or, to adopt James's term plasmoquine may be considered as a "chemoprophylactic." It is therefore necessary to indicate the second point of action for plasmoquine in our diagram, and this I have shown by the second — — — — — line. But we must wait until this work has been completed before the significance of these findings can be correctly assessed. Yet the scientific importance of this work is already definitely established, since it has drawn our attention to many new aspects of the problem which reveal the way to discover new drugs, differing both from quinine and from plasmoquine, which might attack the cycle of development of the malaria parasites at other points.

DIAGRAM VIII.



Plasmoquine Fourneau 710

Recent work in our laboratories in Elberfeld goes to show that these considerations are following the right lines. I shall say a few words regarding them, but first I shall cite briefly what has already been done by other investigators in this field. In America, Hegener, Shaw and Manwell, in England, Barger and Robinson, in conjunction with Macfie and Keilin, have already published their results. In France, Fourneau published in 1931 a paper on a synthetic anti-malarial compound prepared by himself, which he called Fourneau 710 and submitted to clinical trial. Diagram VIII shows the constitutional formula of this body alongside that of plasmoquine; the difference between the two lies in a shortening of the carbon chain.

The experiments of Bramachari in Calcutta have so far given no practical results, while Collier, Warstadt and Krause have not yet communicated the outcome of their investigations.

According to a short communication in the *Sowjetskaya Pharmazia* (March, 1931) the Russians appear to have produced anti-malarial combinations of quinoline which are at present undergoing clinical tests.

In our laboratories in Elberfeld, Mietzsch and Mauss have succeeded in forming new compounds while developing the work on plasmoquine by formulating another heterocyclic ring system; these compounds have been tested in animal experiments

by Kikuth, the head of the Bayer-Meister-Lucius Chemotherapeutic Institute in Elberfeld. Kikuth employed a new experimental method which he evolved and will publish later. By his method he has determined, not only that the new compounds were effective against malaria, but also that this action differed in principle from that of plasmoquine. Kikuth is of opinion that our new product is likely to be effective against the schizonts in the same way as quinine is. And since Sioli showed that the product was effective in inoculated malaria in general paralysis, we have sent supplies of it to a number of investigators in the tropics and sub-tropics for practical therapeutic tests. Our expectations have been realized. The compound acts on the schizonts of malaria and has no effect on the gametocytes. We have no data as yet regarding its effect as a prophylactic.

The mode of action of this new compound again proves that anti-malarial drugs possess specific properties. It may be—and the future alone will show—that the new compound has other potentialities in its action. It seems to offer advantages in dosage and duration of treatment, and also it appears capable of materially reducing the number of relapses after treatment. I have tried to give in general terms the first impressions we have formed regarding the action of this compound in practice. A full account of the details must be reserved for the publications of those workers who are now and will be in future investigating its effects.

I have endeavoured to show how each step has been built up on the results of work done in the past. Based on this ground-work, we may perhaps have added some small contribution to the edifice. Whether the next step will be furnished by other workers or by ourselves is of little moment—all that matters is the advancement of science and the help that can be given to the sick.

Discussion.—Colonel S. P. JAMES: Plasmoquine is the first effective anti-malarial drug that has been prepared synthetically in the laboratory, and Professor Schulemann's decision to come to England to explain in detail the history of its discovery and the exact nature of its chemical constitution was a friendly gesture which I am sure will be fully appreciated in this country. The discovery is noteworthy, not only because plasmoquine is a potent anti-malarial weapon, but because observation of the results of its action on the malaria parasite led to an important change in ideas and aims concerning the chemotherapy of malaria. Formerly it was generally believed that malarial chemotherapy comprised only the single problem of finding a drug which acts more effectively than quinine in curing attacks of the disease, but now it is realized, as Professor Schulemann has explained so clearly in his paper, that the problem is not a single one but includes four items of research, each of which must be considered separately. There is first the problem of the sporozoites; secondly, that of the asexual parasites; thirdly, that of the sexual forms, and fourthly, that of the forms responsible for relapses. Perhaps in the future a drug may be found which will act equally well on all those stages, but at present the conclusion to be drawn from a knowledge of the action of plasmoquine is that a different drug must be used for each stage. For destroying the sporozoite stage plasmoquine is as yet the only known drug with an effective action, but even plasmoquine is not entirely satisfactory for the purpose because, according to our latest experiments, it seems probable that, to secure complete protection from infection in an intensely malarious place, one would have to take more than four centigrammes daily, and even four centigrammes is a dose which might produce toxic symptoms if taken daily over a long period. For dealing with the asexual stage, quinine is already available, and perhaps for that purpose a better product would be hard to find. On the sexual stage plasmoquine acts excellently and in doses smaller than are necessary for destroying the sporozoite stage. Lastly, for the stage that is responsible for relapses there is as yet no known drug which acts effectively. Professor Schulemann has mentioned some reports in which it is stated that the relapse rate after a course of plasmoquine is less than the relapse rate after a course of quinine. I cannot help thinking that the observations recorded in those reports may be open to a different interpretation, and that, at any rate in malignant tertian fever, plasmoquine is not more effective in preventing relapses than is quinine. The diagram [shown] of the clinical course of five cases of malignant tertian malaria treated at Horton is of interest in this connection.

You will see that in all these cases a course of plasmoquine, either when given alone or when combined with quinine, failed to prevent relapses. The cases shown on the diagram are of a severe type, but they exemplify what seems to us at Horton to be a chief difficulty in appraising the therapeutic value of new remedies. The difficulty is that each species of the malaria parasite includes several different varieties or strains, of which some must be regarded as being quite virulent, others quite mild. This is particularly obvious as regards different strains of *P. falciparum*. At Horton we have worked with seven different strains of *P. falciparum*, of which two originated in India, one in W. Africa, one in Sardinia and three in Rome. Quinine in small doses sufficed to cure all the cases infected with the Indian strains, but the cases infected with the Rome and Sardinian strains were very refractory to this drug even in large doses and on several occasions we have been quite at a loss to know how to cure them. The diagram illustrates five cases of that type. The experience shows that before venturing to say that a new drug possesses remarkable curative properties one must first ascertain that the cases on which it is being tried were not infected with a strain which could be cured as easily by moderate doses of quinine.

In conclusion one might say that for malarial chemoprophylaxis the primary need at present is a drug that has the same action as plasmoquine but is somewhat less toxic, and for malarial chemotherapy a drug which when taken in therapeutic doses for a short period will effectively prevent relapses. I gather from what Professor Schulemann has said to-night that one or more new preparations which he hopes will fulfil those requirements may soon be available. We shall look forward with the greatest interest to that prospect, and in the meantime I should like again to express my admiration to him and to his co-workers for the remarkable advances in the chemotherapy of malaria which they have already made.

Sir MALCOLM WATSON said that he hoped for greater things from a drug which would strike at the schizont rather than from one which struck at the gametocyte, and he was keenly interested, therefore, in "erion." He had drawn up a scheme of malaria-control for a large copper mine on the Congo Border well within the tropics, being only about 10° south. Anti-larval control had been so efficient that within two years malaria among Europeans for the month of November had fallen from 78 per 1,000 to 4·8 per 1,000. The number of Europeans was over 1,800. In addition there were over 10,000 Africans, among whom were some 1,500 children. We knew the spleen-rate and the parasite-rate of the different age-groups of the African children. This seemed to him a very unusual opportunity of experimenting with the new drug, because the experiments would be carried out under the enervating conditions of the tropics, which were entirely different from the conditions in England or in the temperate zones.

Section of Urology.

President—Mr. A. Ralph Thompson, Ch.M., F.R.C.S.

[*January* 28, 1932.]

PRESIDENT'S ADDRESS.

Some Points in Connection with the Successful Issue of Simple Prostatectomy.

By A. Ralph Thompson, Ch.M., F.R.C.S.

Abstract.—The patient before operation is trained by an experienced nurse in the art of thoracic respiration.—Deep anæsthesia during the actual enucleation of the growth of the prostate.—The scrotum and penis must be kept well up on the abdomen after the operation, and a suspensory bandage must be provided for the patient on discharge.—1 c.c. of pituitrin is injected immediately after the operation.—The first post-operative dressing is not done for twenty-four hours after the operation. No catheter is used after the operation, except very occasionally. The slightest sign of post-operative disease of the air-passages should be treated adequately, and immediately.

Those of us who have any large experience of prostatectomy know that much of the success of the operation depends upon careful general examination of the patient, in particular of the functionating powers of the kidneys. The operation itself may be easy, but when it has been carried out various precautions are needed for a successful issue.

It is the object of this address to show up details of examination and treatment that have been found useful in twenty-one years' experience of this operation in the genito-urinary department at Guy's Hospital.

No doubt each individual surgeon has a uniform method of treatment, gathered from his own experience, but the operation is so frequently performed by individuals without much experience as to the necessary after-treatment and the precautions which should be taken, especially in the way of intelligent anticipation, that one may be pardoned for drawing attention to points which are probably perfectly well known to many readers.

The examination of the patient should never stop with the chemical investigation of the renal function. Let us take, for example, the condition of the chest. I do not wish to convey that pneumonia after prostatectomy may not be really renal in its origin and progress, but a deficient thoracic respiration may lead towards the development of such a condition.

The points to which it is desired that attention should be directed may be classed quite simply: (1) The condition and treatment of the patient in the period before the operation. (2) Some details of the operation itself, and finally (3) the treatment after the operation.

Before the operation.—There is no difference between the pre-operative treatment for suprapubic—and that for perineal—prostatectomy.

As a rule it is a good thing to get the patient accustomed to his surroundings. The renal function has to be studied, and this takes some time. Meanwhile, examination of the various organs should be made, and in particular of the powers of thoracic respiration. Old men almost invariably have got into the way of using only their diaphragm—a fatty great omentum is evidence of this. A man with a large abdomen is a poor thoracic breather. The omentum may be considered to become fatty in advancing life to give the diaphragm something to contract against, for the abdominal muscles do not at this period of life give much assistance.

We are accustomed to hear of the barrel-shaped chest of the emphysematous individual, but almost of greater importance is the bowing of the upper part of the thoracic region of the spinal column.

It is my invariable rule that the sister-in-charge of the massage department should instruct patients who are to undergo prostatectomy in thoracic breathing. She uses much the same massage and instruction as is used in cardiac cases. I was much impressed the other day by the efficacy of her treatment before the operation in the case of an old man. After the operation one was able to show the dressers how well he was using most of the thoracic muscles as well as the diaphragm. Such a patient could hardly have contracted pneumonia after the operation.

It has always been a cause of discussion as to whether or not the catheter should be used before the operation. As a matter of fact it is frequently used in the out-patient department, previous to admission, as I cannot think that a catheter passed under modern conditions does any harm, and it may do much good in relieving the kidneys of much strain. It is a constant source of delight that so few cases of infection of the bladder by means of a catheter have occurred at Guy's Hospital. I doubt whether more than one case has occurred since the genito-urinary department was established there in 1910.

I would insist, however, that strict asepsis is required, but, in my opinion, of far greater importance is the absence of damage to the urethra especially in the prostate region, as without damage sepsis is unlikely to occur. If damage be done to the urethra in this region I believe that the question of a future operation of prostatectomy becomes extremely grave.

The judicious use of a catheter has, however, other advantages than relieving chronic retention—local conditions of the penis and urethra are not missed.

I recall two important cases in this connection:

(I) In the first the patient was a man aged about 65. The medical man who called me in could not pass any instrument at all. The condition of the end of the penis was congenitally abnormal. There was slight hypospadias, and as is commonly the case the apparent opening was not the real one. There was a deep pit in the usual place of the meatus, but the real opening was some distance behind this and was quite small. I passed an instrument quite easily. He was operated upon by someone else, and I was told that the operation was not quite a success as a prostatectomy, perhaps owing to the nervous condition of the patient, but I wonder whether the exact condition of affairs was ever appreciated by the other surgeon.

I have been called in after a prostatectomy because of a fistula, and I have been struck by the filthy condition of some of the foreskins and adjacent parts that I have seen. If circumcision is not performed, it is the duty of the operator to see that these parts are as clean and normal as possible.

(II) In the second case the patient was a man aged about 70, who in his youth had been very alcoholic. He had had a stricture of the urethra, but undoubtedly the main trouble was caused by an enlarged prostate. After prostatectomy, he went on well for ten

days, then started to spit blood, and had signs of an embolus in the right lung. He recovered from this and then developed right femoral thrombosis. Later he got left femoral thrombosis. I was anxious about him, and as I was going home one night I suddenly thought of certain figures that I had worked out in connection with the association of syphilis and gonorrhœa. I had found that twenty per cent. of venereal cases at Guy's Hospital had both syphilis and gonorrhœa, and I asked myself whether mercury might not be the drug indicated rather than those which had been ordered. I went back at once and ordered mercury. It acted marvellously, the patient being better the next day; he rapidly recovered, and I knew him to be well seven years after the prostatectomy.

If then, with a catheter, a stricture is discovered, it might be useful to give mercury to prevent complications due to syphilis which might be lit up as a result of the operation. I certainly should do so.

The local conditions, congenital or acquired, must be studied thoroughly before the operation. Intelligent anticipation of possible conditions are so much better than attempted cures in an elderly or old man.

My consulting room is now on the first floor; to me this is an immense advantage. If the patient has anything wrong with his chest the one flight of stairs affects his breathing, and he is not likely to be a good subject for prostatectomy.

With regard to the anæsthetic, I am a little suspicious of atropin for old men as I fear it may tend to produce an ileus. Before operation I insist on the absolute cleanliness of both foreskin and glans.

At the operation.—I tell the anæsthetist that I like the patient to be deeply under while the adenoma of the prostate is being removed. A mild antiseptic fluid is injected into the bladder till it can be palpated above the pubes ; no fixed quantity of fluid can be used, the palpation of the bladder is the important point. The catheter is removed and a loose india-rubber tourniquet is placed round the base of the penis, above the scrotum, and secured lightly. This tourniquet is removed directly the bladder has been opened.

The bladder is then cut down upon. When it is exposed some gauze roll is placed carefully and deliberately round the exposed bladder, and as deeply as possible without too much of the surrounding area being exposed.

The bladder is then opened transversely, first because the longitudinal veins on the bladder wall are cut completely across and not nicked as they may be with a vertical incision, hence there is much less bleeding than if the incision be vertical. A Lane's clip forceps is placed upon the upper edge of the bladder wound until it is enlarged in both directions.

The second reason for the transverse cut is the position of the peritoneum, which can be stripped much more easily from the sides of the bladder than in the mid-line where the urachus is situated. Thus the danger of wounding it is much more easily avoided. The question of going on with the operation if the peritoneum be wounded must depend on circumstances, but I should recommend strongly immediate suture of the peritoneum. I have only once wounded it in prostatectomy, and then the intestines came down after the bladder had been opened, so if there was a chance of infection it had already taken place.

Before operating on the prostate itself the interior of the bladder should be carefully explored.

I have found stones, and this possibility is well known ; but not so well known is that of the presence of a papilloma of the bladder, of which I have had at least three cases in association with an enlarged prostate. A sacculus may also be missed unless the bladder be explored. The recognition of a sacculus should be regarded as important, especially if it be directed down towards the groin, for then it may be associated with an inguinal hernia and cause trouble. Moreover, it will cause more trouble if the bladder should become septic after the operation.

Then the adenoma or adenomata of the prostate are removed. The prostate may

be pushed more prominently into the bladder by an assistant pressing firmly with his hand in the perineum. Usually there is little bleeding, but if there is, it must be stopped by the surgeon on the operating table, for if he cannot stop it, the house-surgeon is no more likely to stop it when the patient has gone back to bed; for this, we have always open to us the method practised by Sir John Thomson-Walker. But I am not sure that every surgeon is able to follow his plan, nor may the condition of the patient allow of it. Short of this, much good can be gained by plugging the cavity from which the abnormal prostate has been removed, and if necessary, the bladder cavity itself.

As much as five and a half yards of ordinary cyanide gauze may be packed into the bladder. The rectum may also be packed.

But I believe that the cause of my having at Guy's Hospital at present very few cases of serious hæmorrhage lies in the massage of the prostatic cavity by myself and by all the dressers who are in the theatre helping me. They learn exactly where the prostatic cavity is, and this is very important from the point of view of drainage and other after-treatment. The way in which a massaged cavity contracts down is quite dramatic, and such cavity may grip the examining finger quite tightly. I also

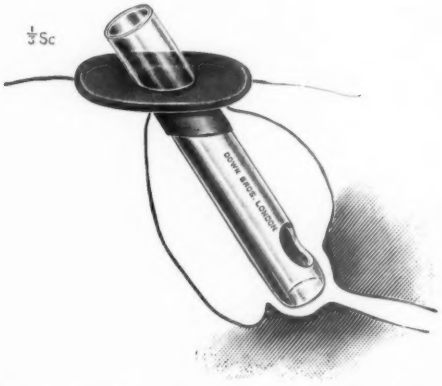


Diagram of flanged drainage tube in region of prostatic cavity after removal of an adenoma.

use very hot liquor hamamelidis, B.P. strength, of a temperature of at least 110° F. The gauze roll is removed from round the bladder, and if there be no bleeding the bladder is allowed to fall back into its true position. I think that an anatomically correct bladder is likely to have a much more natural physiological function than one that is kept in an abnormal position.

Drainage is important; if the bladder is not the seat of inflammation I do not want to drain it, but I do want to drain the cavity from which the prostatic growth has been removed. If the bladder is septic, then the drain used for the prostate region will drain the bladder, but it is a prostatic drain not a vesical one. The drain should be directed downwards and forwards, and led into the cavity from which the growth has been removed. For this purpose Messrs. Down Bros. kindly made for me a glass tube with an oblique flange. That, in my opinion, is the way to use the tube for drainage.

We now come to the question of the material to use for the tube. I have had india-rubber long under suspicion, and have given it up, except for this flange, and

that is kept off the wound by dressings. Professor Gibson tells me that india-rubber usually contains free sulphur; sulphur has its uses in urinary surgery, but it is not wanted now. I tried asbestos tubes, but they tended to become flabby and messy, so I have given them up. I now always use glass tubes.

Everything being as normal or possible, I put in superficial sutures through skin and rectus sheath, taking particular care not to go through the rectus muscle, and by these sutures the edges of the wound are approximated. I think there is real danger of wounding the peritoneum—which is now in its normal position—if the sutures perforate the whole thickness of the rectus muscles. I do not put any suture through the skin in the lower part of the wound. A former house-surgeon of mine, Mr. D. J. P. O'Meara, taught me that such a suture led frequently to local œdema. I believe that this observation is correct.

The dressing is then applied, but one very important step must be taken—the scrotum and penis are brought as high as possible on to the abdomen and kept there till the patient is allowed to get up. It is a great delight to me to see my patients in Guy's Hospital with rugose normal scrota, and a penis that is not swollen.

The patient being now ready to be taken back to bed, 1 c.c. of pituitrin is injected. This is one of the most important points I have mentioned so far. The house-surgeons use it now as a routine, and are convinced of its efficacy in preventing bleeding and shock. As a preventive of either this dose is quite sufficient. As a cure for certain after-operation conditions the dose must be larger.

One of the proudest moments of my life was when a valued colleague in the same line of practice told me he was anxious about a patient who was threatening an ileus, and asked my opinion. I suggested that 2 c.c. of pituitrin should be injected, and I was even more proud when he informed me that it had acted like a charm.

After the operation.—After the operation the patient is not dressed for twenty-four hours. If the dressings get saturated with sanguineous urine they are packed, but not removed. Morphia may be given to ensure rest, if not sleep, the first night. I need hardly say that at the operation dressing, the parts should be very carefully cleaned; ether is most useful and may be used sparingly, with precautions as to a free flame. But dried blood must be removed. Then at the first dressing after the operation any accumulated blood can be easily removed. The scrotum and penis must be kept raised. After the first post-operative dressing the exhibition of one ounce of neat brandy is indicated as a routine practice ten minutes after the dressing has been completed, when the patient is comfortable.

These precautions are taken, for the patient should be kept as quiet as possible immediately after the operation since there is a good deal of shock when the first post-operative dressing is being done.

We now come to a more debatable point, namely, the use of a catheter. Dressers frequently ask me when I take the catheter out after a prostatectomy; I reply that I do not as a rule place one in the bladder.

John Hunter long ago pointed out that with urinary fistulæ a catheter was a foreign body and subject to all the rules of foreign bodies. I feel most strongly that this is the case when a suprapubic operation has been done. A catheter tied into the bladder requires most careful attention, and even then may be a source of sepsis. Moreover, it limits the movements of the patient, and this makes for lung complications. Therefore for local and for general reasons the catheter is not used unless its use becomes necessary at a later period for the closure of the wound. I recollect a case of a man upon whom I had operated for doubtful malignancy of the prostate gland and had removed the organ.

This took place at Easter; at Whitsuntide of the same year I was asked to see him as the wound had not quite healed up, though it was reported that there were

good "granulations." He leaked at night, but was dry during the day. I found him sitting up in bed. When I examined him I found that the "granulations" were not so in fact. The mucous membrane of the bladder was being pushed into the wound so as to form a valve, and during the day, when the patient was sitting up, it most efficiently kept the water from flowing through the fistula, but when he lay down at night the weight of the viscera was taken off the bladder and allowed the mucosa to sink back, and thus permitting the flow of urine. Let me emphasize this point. I have so often seen it deceive even the most assiduous dresser. It is partly for this reason that I allow the bladder to sink back into its normal position after the prostate growth has been removed. If after about a fortnight without a catheter, there is little sign that the wound is making final efforts to close, I get the patient up for two days and warn him that he may have to go to bed again, but that he must not be discouraged by this. After the two days he is put back to bed with only one pillow.

This position prevents the viscera from weighing down the bladder through the wound, but there is another most important point. I learnt it from my first house-surgeon, Mr. Le Vieux, now of Mauritius. He had observed that a well-marked abdominal line of flexion ran across the suprapubic wound, and opened it up about its middle. The observation is quite correct. So to get rid of this line of flexion the patient is laid on his back and a catheter inserted, and the wound usually closes in about three days. I now quote three cases of suprapubic prostatectomy, in which no catheter was used by me and not at all in two of the cases. The first two were in Guy's Hospital at the same time; both were men aged 68. In the one case the bladder wound was soundly healed in fourteen days, and in the other it was healed up in thirteen days, both without the use of the catheter.

The third case was a man just under 60; he was anxious about himself and his work, and was not quite an ideal patient from this point of view. Nevertheless he made an extremely good patient, and had no catheter inserted by me, and went out in about five weeks with the wound soundly and permanently healed. For some reason, not clear to me, he went to another surgeon, who passed a catheter, and the patient at once got an orchitis, from which he has completely recovered. I believe that a catheter, unless very carefully attended to, does tend to produce an orchitis.

The drainage tube is taken out in my practice directly there is no sign of blood or pus in the washings. It is then left out altogether.

I find boracic crystals most useful; since I have used them, on the advice of Mr. Swift Joly I have not been anxious about the local state of suprapubic wounds. The powder must not be used; the wound should be filled with the crystals. The use of these crystals has quite altered my former views of the nasty sloughs that one used to see. These sloughing processes cause great anxiety, however. I am sure about many things in connection with them. First, and especially when they are grey or dark in colour, undoubtedly they show a very weak condition of the patient, and may be a sign of approaching death. But in any case two important points must be attended to, namely, most assiduous care must be taken to keep the parts acid; very dilute glacial acetic acid may be used for this purpose, but boracic crystals are better. Secondly, they are staphylococcal in origin. I believe that when a boil is to be treated by the surgeon it should be simply laid open, but no pressure used to get rid of the slough, for the poison is only pushed into adjacent parts and may do much harm. Similarly with sloughing wounds after suprapubic prostatectomy, the slough should always be allowed to come away of itself and never be detached from the wound, unless quite loose.

These sloughs may affect the bladder itself; they may be dangerous to life and they always prolong healing. I hope I have seen the last of them. The fact that I have seen so very few, if any, in recent years leads me to suppose that some of the forms of treatment that I have indicated may be useful to other surgeons.

Lastly, as orchitis may be a late complication sometimes occurring even after the patient has gone home, I always now provide a suspensory bandage fitting tightly but not rubbing the scrotum, directly the patient is allowed to walk about.

I will now consider certain aspects of prostatectomy.

First, the question of a complicating stone or collection of stones; I have been brought to think that when there is an enlarged prostate without retention of urine, but with considerable pain, a stone is also present, but such stones may have a renal origin. Therefore the whole urinary tract should be X-rayed to discover renal or ureteric stones. From an examination of several stones, I have concluded that though there might be no clinical evidence of a renal stone, yet the structure of the stone in the bladder indicated that it must have had a renal origin.

My house-surgeon and I proved this point when an elderly man with a large prostate and stones in the bladder was operated upon as a last resort, as he was suffering so much pain. I had the bladder opened by the house-surgeon, and he removed the stones but did not remove the prostate. The man gradually sank, and died. At the autopsy we found oval stones at the lower end of the left ureter; these were undoubtedly being passed into the bladder and formed there the nuclei of larger stones. In some cases single stones have several renal nuclei. The lesson to be learnt from this is that we must not be too hopeful about the success of an operation for the removal of the enlargement of the prostate, if it be accompanied by stone.

Another point of importance in the prognosis is that there may be other conditions present, though the enlargement of the prostate may be responsible for the main symptoms. I remember a case under the care of one of my colleagues; he had a carcinoma of the colon, chronic Bright's disease and an enlarged prostate. This man might have gone to a general surgeon, to a urinary surgeon, or to a physician. Whatever course he had pursued the prognosis was not good. Carcinoma of the rectum should always be excluded before operation for an enlarged prostate. I have seen two cases in whom both these conditions were present.

Diabetes.—Under present conditions I do not think that the presence of glycosuria contra-indicates removal of the enlarged prostate. I have had two successful cases in which the patient was placed on a suitable diet; both patients are very well at present, though of course insulin treatment would be indicated strongly.

I now come to a point of real importance: In the hospital it is usually easy to get wives of patients to keep away from their husbands for two or three days after the operation. I am sure that the presence of the wife does harm to the patient; if this is explained to both before the operation there is usually no difficulty.

Chest complications.—Although no doubt many of the post-operative cases of pneumonia are really of renal origin, I think that intelligent anticipation is the important point. I recollect well Sir Charters Symonds telling me that in certain head injuries, if you waited for symptoms you usually waited till the patient was dead. I also recollect that a question used to be asked at medical examinations as to the signs of post-operative pneumonia. My own feeling is that if you wait for signs you will find them only in the death of the patient. You must anticipate them. Here I would protest against the administration of the latest advertised chemicals, especially alkaloids.

I knew one case in which the house surgeon gave many alkaloids in succession, as the symptoms arose, which, in his opinion, demanded them. When I saw the patient I was hopelessly at sea. Know where you are after prostatectomy, and to know where you are you must have some definite idea when certain drugs may be indicated.

There is cause for anxiety if a patient has a slight huskiness of voice. If this occurs I regard the case as potential pneumonia and give preventive drugs, such as strychnine, ammonium carbonate and potassium iodide.

The old-fashioned steam kettle—used as a preventive, not as a cure—does undoubted good if only the patient does not get anxious because it is being used.

Now we may consider the position of the patient after operation. As I have urged frequently, I do not use a catheter, hence the patient is free to lie in any comfortable position. Such a position is best for him as then his organs act easily and smoothly. I see no reason why a patient without a catheter should not lie on his side. There are some few exceptions to this suggestion. When one is a little anxious about bleeding, the patient may lie in bed with his lower limbs and chest sloping downwards from the buttocks raised on a hard pillow; this position has much anatomical merit.

When the patient is lying in bed after the operation, the cavity from which the enlargement of the prostate has been removed is almost the lowest part of the body. We should not allow a bleeding limb to hang down—why should we allow a bleeding prostatic cavity to do so? We should raise the limb, and we must raise the prostatic cavity, especially as there is some shock, with all its paralysis of the vaso-motor nerves, to make the bleeding all the worse.

When it is desired that the wound should finally heal up, the patient may lie on his back as flat as possible.

It is most important that sleep should be procured after these operations. I have seen no particular good from any other drug than morphia, and I use it if it is needed.

With regard to the operation that I call primary union prostatectomy, I have performed this in a good number of cases since I gave an address here years ago on its advantages, and I have not altered my opinion upon it. The question of operating for the removal of an enlargement of the prostate during an attack of acute retention is important. It may be difficult to get all the chemical tests connected with the renal functions made, but if one is satisfied with the clinical condition of the patient it may be that such a procedure is justifiable. No time is lost with distension of the bladder, and the patient is probably not averse to the operation being done.

Early operation is good; we know enough of the natural history of the enlarged prostate to be able to forecast the progress of a case. One must recollect that one of the early symptoms of prostatic enlargement is irritation in the region of the base of the bladder. When a man has such a symptom, but no retention, though we know that such a condition will arise, I think we are justified in advising the full operation. I have had most successful results from early interference and removal of the enlargement of the prostate. There is perhaps too much importance attached to the obstructive symptoms rather than to the actual fact that there is new growth there, even though of a simple pathological nature.

I have never regretted doing an early operation, and have removed quite small adenomata from the prostate with very beneficial results.

Pre-operative alkaline treatment.—In many cases the administration of sodium bicarbonate before operation is indicated, but I have no time to deal with this important question here.

Discussion.—Mr. MORTON WHITBY: From my experience while Resident Medical Officer at St. Paul's Hospital, where a fair number of such cases were under my care, I observed that morphia, one-sixth of a grain before operation and one-quarter of a grain after operation, produced an inhibitory action to the cardio-vascular system and secretory function of the kidneys, where the tests were not good, and in several cases where they were supposedly normal. The clinical phenomena were exhibited by mild attacks of embolism, uræmia and ileus which I attributed to the immediate use of morphia before and after the operation.

Prostatectomy causes considerable shock to the patient, therefore one does not desire to add to this shock by inhibiting the vital systems of the body when they are at their lowest ebb. Pituitrin and frequent hot silver nitrate irrigations will control hæmorrhage, and mist. aspirin co. will alleviate sleeplessness quite as well as morphia. Therefore, I consider morphia absolutely contra-indicated in all cases of prostatectomy.

Mr. H. P. WINSBURY-WHITE: With regard to passing a catheter or cystoscoping in cases of prostatic enlargement for diagnostic purposes, I omit these procedures unless I am not sure of my diagnosis. To pass a urethral instrument in prostatic cases will lead occasionally to acute retention, which is most undesirable and is avoidable if the instrumentation is omitted. I think, however, that cystoscoping the patient on the operating table is a good practice if cystoscopy is considered necessary. I was interested in the President's remarks about his cases of papilloma of the bladder and simple enlargement of the prostate. I have had three or four such cases, and as a result have made the rule, when hæmaturia is a recurring and outstanding symptom in the patient's history, to carry out cystoscopy if possible.

With regard to controlling hæmorrhage, only slight bleeding occurs following the second operation in two-stage prostatectomy. I cannot recall any such case in which I had to deal with bleeding or in which I had subsequent anxiety over loss of blood. The explanation, I think, is that, as a result of the preliminary cystostomy, there is a diminution in the congestion of the prostate with a consequent reduced tendency to bleed. Two-stage prostatectomy is such a life-saving procedure in certain cases, that I think it worthy of mention, especially as we have heard a good deal about chest complications. These in my experience are of the rarest possible occurrence, following the second-stage operation.

I am sorry that the President objects to the simple procedure of vasotomy. It is a most effective preventive of post-operative epididymitis, a most unpleasant complication which may have a considerable influence on the ultimate course of the convalescence, to say nothing of the fact that even months after discharge from hospital epididymitis sometimes occurs.

I am interested to hear that the President sometimes carries out prostatectomy in cases with acute retention. I would be afraid to do this, as my experience is that these patients do better with preliminary indwelling catheter drainage.

Mr. E. W. RICHES said that he was at present engaged in following up prostatectomy cases of different surgeons, extending over a number of years, and the outstanding impression he had gained was that the simplest operative and post-operative procedures gave the best results. He had seen several cases of late epididymitis, and one case after division of the vas without ligature; on the ligatured side there was no epididymitis. He was in favour of routine cystoscopy when it could be easily performed; in cases in which elongation and angulation of the prostatic urethra made it difficult, the attempt should not be persisted in. He regarded the clinical condition of the patient as of greater importance than the result of laboratory tests in deciding for or against one-stage prostatectomy, and he considered acute retention a contra-indication.

Mr. F. MCG. LOUGHNANE: Sufficient emphasis has not been laid upon the importance of routine cystoscopy and urethroscopy as a preliminary to suprapubic prostatectomy. Urethroscopy will reveal a stricture, and it is essential to treat this before the suprapubic wound will heal. Cystoscopy will show the presence or absence of calculi and papillomata, and will give some idea of the state of back pressure on the kidneys, and also the degree of sepsis or cystitis present. Making a large wound in the bladder for investigation purposes is, therefore, not necessary, and the simple Freyer operation can be performed with advantage to the patient. The "open" operation for enlarged prostate in old men is not always the best, for the extra time involved increases the shock, and the kidney function is never good.

Section of Dermatology.

President—Dr. A. M. H. GRAY, C.B.E.

[*January* 21, 1932.]

? Lupus Erythematosus.—NORMAN BURGESS, M.D.

H. P., a girl aged 11.

History.—At the age of 7 an erythemato-squamous eruption appeared on the left ala nasi and on the dorsal surfaces of the distal phalanges. There was some desquamation of the palms and palmar aspects of the fingers. Since then similar patches have appeared on the scalp, the concha of the left ear, and the upper lip. The vermilion border and mucous membrane of the lips are also involved. The patient has been under my care for about a year. During this time there has been no change in the situation of the eruption, although the condition is usually somewhat worse in the winter. One uncle died from phthisis.

Report of X-ray examination.—"No sign of active tuberculosis in the lungs, but rather more healed foci in and around the hilar areas than normal. Probably these foci are situated in the lymph nodes."

Local applications of sulphur, salicylic acid, and resorcin produced no improvement. Three doses of 0·01 grm. and one of 0·02 grm. of sanocrysin were given in November, 1931, but there was no noticeable effect on the eruption.

Comment.—In view of the situation, persistence, and appearance of the lesions I suggest a diagnosis of lupus erythematosus.

The recent paper by Cummer (*Arch. Derm. and Syph.*, 1931, xxiv, 999) seems to indicate that this disease is not so rare in childhood as many authorities have stated.

Discussion.—Dr. L. FORMAN said it seemed to him that the condition was psoriasis. The lesions on the hands were sharply limited and dark red in colour, suggesting psoriasis of the palms. There was a circumscribed scaly area on the scalp, and the scales were easily detachable. Removal of scales did not cause pain, and there was no bleeding.

Dr. BURGESS (in reply) said that the diagnosis of psoriasis had been considered, but he thought that it could be excluded. The patches had been persistent and unchanged in appearance, in the same situation on the face and hands, for four years. He did not agree with Dr. Forman that the scales were easily detached; he thought that they had already been disturbed when Dr. Forman examined the patient.

Multiple Erythematoid Benign Epitheliomata. — Sir ERNEST GRAHAM-LITTLE, M.D.

This is a case of multiple basal-celled epitheliomata of very benign behaviour. There are five lesions altogether, in different stages of development; some in the phase of the superficial seborrhœic type, some with the later development of the

small pearly nodules, and one with a definite nodular growth. That last lesion is probably a product both of the disease and of the treatment, because it was diagnosed as lupus and treated with caustics ten years ago. Most of the lesions are at least a year old. The odd distribution in this case is on the dorsum of the foot; I have not seen it before in that situation.

Xanthoma Diabeticorum.—Sir ERNEST GRAHAM-LITTLE, M.D.

This is a case of diabetes with extensive xanthoma, with yellow papules, characteristically distributed in the lines of cleavage of the palm, and on the elbows where the nodules are large. The patient is aged 16, and is employed in the Post Office. Dr. Turtle has been able to control the sugar by dieting, and consequently dieting is the only form of treatment that the boy has had. There is an amazing amount of cholesterol in the blood, namely, 750 mgm. per 100 c.c. of serum, or five times as much as it should be, and there is a pronounced glucose-tolerance curve. There is no serious constitutional illness, and on the whole, the patient seems to be keeping well. But his condition is a bar to his promotion, and the question is whether he should not therefore be put on to insulin.

Discussion.—Dr. H. W. BARBER said he believed that xanthoma was always associated with a high cholesterinæmia, but not necessarily with glycosuria or hyperglycæmia. His view was that the lesion of true xanthoma diabeticorum was usually a reddish papule with a yellow top. One would scarcely expect an anti-diabetic diet to affect the xanthoma.

Dr. NORMAN BURGESS said that a few months ago he had had a closely similar case. He had diagnosed his own case as one of xanthoma tuberosum multiplex, and on investigation the patient was found to have lipæmia, but the resting blood-sugar and the reaction to the glucose tolerance test were normal. Although cases of xanthoma diabeticorum were said to respond to insulin, Ingram (*Brit. Jour. Dermat.*, 1927, xxxix, 335) had found that in a case of xanthoma tuberosum multiplex the hypercholesterolæmia was unaffected by insulin.

Dr. J. A. DRAKE said that, in his opinion, the majority of cases of xanthoma were not associated with sugar in the urine or with a high blood-sugar curve. The present happened to be a chance case in which the two conditions were associated. He agreed with Dr. Barber that the lesion in the true diabetic case was more vivid than that seen here.

The PRESIDENT said he agreed with Dr. Barber that the red type of small nodule was that most commonly associated with diabetes, though he did not agree that this type did not occur apart from cases of glycosuria. On many occasions he had seen the bright red type of lesion when there was no disturbance of the blood-sugar curve. He believed that there was no essential difference between the two conditions and that both were due to the same cause, namely, a disturbance of the lipoid mechanism.

Dr. G. B. DOWLING said that recently he had had experience of two cases of xanthoma with multiple nodules, both in diabetic patients. One, seen three years ago, was in a man aged about 50. On a strict diet the xanthomatous deposits cleared up gradually, and the patient was now free from them.

In the other case, seen about nine months ago, and since then thoroughly investigated at Charing Cross Hospital, the xanthoma had persisted for a long while in spite of treatment with insulin, but was now clearing up. He thought that probably the lipoid content of the blood diminished more gradually under treatment than did the sugar, and that only gradual resolution of the lesions was to be expected.

He had supposed at one time that excessive lipoid in the blood in a diabetic was of serious significance, yet in cases of xanthoma diabeticorum the patients often appeared to be in better general health than the usual run of diabetics. He would have expected so marked a disturbance of fat metabolism to be associated with acetonuria at least, but in his two cases this had been absent. [Sir ERNEST GRAHAM-LITTLE: It is present in this case.]

Dr. F. PARKES WEBER said he thought that the eruptive xanthoma in this case, although without a reddish tinge, might be ætiologically connected with the diabetes mellitus—probably, however, it was not the most acute variety of diabetic xanthoma. He would suggest

a trial of the effect of insulin treatment on the xanthoma, if the blood-sugar was found to be still above 0·1%.

The PRESIDENT referred to a paper by Udo Wile on the dietetic treatment of non-diabetic xanthoma, from which it appeared that dietetic reduction had to be so severe that it was necessary to keep the patient in bed to get the lesions to disappear. As soon as the diet was increased sufficiently to allow the patient to work, there was a return of the lesions.

Sir ERNEST GRAHAM-LITTLE, in reply, said he was interested in Dr. Barber's suggestion, and asked whether it was thought there should be two classes of xanthoma, the red and the yellow.

Dr. BARBER said he agreed with the President that in the majority of diabetic cases, the xanthoma lesions were of the pink type. He would have called this xanthoma tuberosum, and he did not associate this necessarily with glycosuria or a high blood-sugar, but always with a high cholesterolæmia. In a child under his care, with extensive xanthoma of this type, the blood-sugar was normal, but the blood-cholesterol was very high.

Eczema of the Tongue: Geographical Tongue.—C. H. WHITTLE, M.D.

Mrs. L., aged 70, gave a four months' history of pain, irritation and burning on the left side of the tongue, especially associated with the taking of food.

There is a well-defined scaly edge to the inflammatory process which is slowly advancing, leaving a smooth shiny atrophic surface. The process appears to be quite superficial. There is a recurrence in the healed part at one spot, presenting the same scaly edge as the margin elsewhere.

The patient has had some dyspepsia of an atonic type and she still shows evidence of anæmia. The dyspepsia has improved since the removal of her few remaining septic teeth. The Kahn reaction of her blood is negative.

Bacteriological examinations of scrapings from the edges of the lesion show a large number of Gram-negative diplococci roughly kidney-shaped, and in the cultures on ordinary blood-extract media these organisms are overwhelmingly predominant. They ferment glucose, lævulose, saccharose and maltose rapidly, and so would appear to belong to the *M. pharyngis siccus* group. The colonies are, however, not those of *M. pharyngis siccus* and are smaller, more delicate and moister.

Treatment.—Various mouth washes, painting with 1% phenol and 1% silver nitrate have had little effect. Mercury and potassium iodide by the mouth have also failed to influence the lesion.

A vaccine has been made from the Gram-negative coccus, but intracutaneous injection of twenty million gave no appreciable local reaction.

Discussion.—The PRESIDENT said there was no doubt that this was the variety known as "geographical tongue," but that term did not settle the question of the ætiology. Because it did the patient no harm, that was no reason for not trying to find out its cause. Much work had been done in the last few years, particularly in regard to the surface bacteriology. It was possible that it was a surface infection, and it might equally be a figurate erythema. He assumed that Dr. Whittle had excluded, as far as he could, the possibility of fungus or yeast-like organisms being present, as these were thought by some to be responsible for some cases.

Dr. J. M. H. MACLEOD said that he had investigated cases of geographical tongue for fungus of the monilia type, with negative results. He had come to the conclusion that true geographical tongue was connected with some digestive disturbance, and corresponded somewhat to a toxic figurate erythema of the skin.

Dr. WHITTLE (in reply) said that he had twice examined the scrapings from the edge, and had been unable to find anything but the large cocci. Those cocci were more delicate than the ordinary saprophytic organisms found in the mouth, and they gave the sugar reactions of a group which was not the ordinary pathogenic group, like the *Micrococcus*

catarrhalis. In none of the examinations had he found a fungus. As Dr. Barber had said to him (in conversation), in fungus infections of the mouth the fungi were either present in large quantities or were entirely absent.

Adenoma Sebaceum.—JOHN FRANKLIN, M.B.

This patient, Mrs. A. M., aged 33, married, has had the condition on the face as long as she can remember. She suffered from epileptic fits from the age of eight until two or three years ago. Last October she had a miscarriage and during the pregnancy had three further epileptic fits. Otherwise she is perfectly normal, enjoys good health and is intellectually bright. The Wassermann reaction is negative. She states quite definitely that if she becomes ill the condition of the face improves and she is certain that some years ago during an attack of pneumonia the whole thing disappeared for a short while. She has two sisters quite normal, but she thinks that her mother had a patch similar to her own on one cheek.

On examination numerous small soft white tumours, varying in size from that of a pin's head to that of a lentil, are seen on the nose and both cheeks, being most marked in the furrows on either side of the nose. There is no abnormal pigmentation, and, except for an occasional dilated capillary, there are no marked telangiectases. There are no moles or other tumours to be seen. Dr. Pulvertaft, of Westminster Hospital, has kindly prepared the microscopic sections and reports that:—

"The tissue consists of proliferated sebaceous glands which project more deeply than normally into the corium. The ducts are in places blocked forming cysts. There is chronic inflammation and blood-vessels are prominent. No sign of nævoid cells."

The condition, I take it, is one of simple adenoma sebaceum, similar to the case originally described by Balzer and Ménétrier (*Arch. de Physiol.*, 1885).

Discussion.—Dr. F. PARKES WEBER said he thought that this case was really one of Pringle's telangiectatic type of adenoma sebaceum, in spite of the lesions on the face being less red than they were in most cases. The fits spoken of might have been true epilepsy, and they suggested that the adenoma sebaceum might be associated in this patient (as it notoriously not very rarely was) with tuberous sclerosis of the brain—an association sometimes termed "epiloia" in England.

Dr. S. E. DORE agreed with Dr. Parkes Weber that this case was of the more common Pringle type. He had seen very few cases of the Balzer or of the warty type. He asked whether Dr. Franklin could state the proportion of these cases who were mentally defective, and whether the cases seen in hospital with a normal mentality were the exceptions. The late Colcott Fox drew attention to the prevalence of the condition in imbeciles.

Dr. C. J. C. EARL asked whether Dr. Franklin had made observations on this patient's mental state, also whether she bore any of the stigmata of degeneration. He (the speaker) had not seen this patient, but from the description he judged the condition to be the classical one seen among mental defectives. In Caterham Mental Hospital there were now fifteen cases of adenoma sebaceum, two of them of the definitely fibromatous type. Most of the patients there showed the bright red telangiectatic type, and the lesions tended to be confluent. Psychiatrists knew this mental condition as epiloia, not a disease but a syndrome; of it, epilepsy was one of the cardinal symptoms. These patients often had had fits for years, and after a long interval they recommenced having them.

Dr. FRANKLIN in reply said that with regard to the mental aspect of the case, Dr. Macdonald Critchley had seen the patient and he, the speaker, intended to send her to him for fuller examination. Dr. Critchley had told him that there were a number of these cases in asylums.

Ichthyosis with Familial Tylosis and Multiple Rodent Ulcers.—ARTHUR BURROWS, M.D. (for DR. W. J. O'DONOVAN).

George W., male, aged 56. Lavatory attendant. This patient has always suffered from a dry, scaly skin, and from thick skin of the palms and soles.

Until he was aged 21 watery blisters appeared at frequent intervals on his body and arms, when they almost stopped appearing. From the age of 21 onwards a tendency to form warty growths on the body developed, particularly on the hands. Usually the warts disappeared in time. Eleven years ago the warts on back of the left hand ulcerated. The little and ring fingers of the hand were removed for the growth, together with the epitrochlear gland. The report of the pathological examination gave a diagnosis on sections as follows:—

(*a*) Piece from edge of the ulcer: squamous and horny carcinoma. (*b*) Another portion of skin: ichthyosis. (*c*) The gland: chronic inflammation.

No lesion ever appears on the face.

Family history.—There is no history of any skin malady in grandparents, parents, uncles, aunts, brothers or sisters. The patient's range of knowledge of these relations is, however, limited. The wife's family history is also clear.

The patient has two children only, both daughters. Both have rough skins, particularly at the flexures, and heaped up, thickened skin of the palms and soles. Both have soft skin on their faces, and good complexions. Neither of them has warty tumours, but their ages are now only 18 and 16 years respectively. They do not manifest blister formation.

Present condition.—The patient's skin as a whole, except on the face, is rough, dry and superficially thickened. The roughness is most marked at the flexures, where the thickening tends to become linear, while very great heaped up, smooth horny thickening of the palms and soles is present.

Scattered all over the body and limbs are numerous keratoses, and in other places are slightly scaly and thickened red areas of skin resembling Paget's eczema, varying in size from 1 to 10 cm. in diameter. A few of these lesions are ulcerated.

On the abdomen, as the result of the changes occurring at the site of a previous warty growth, a large ulcer has developed, about 5 by 4 cm. in size. The ulcer is about 1·5 cm. deep, and has rolled edges with slight induration. No enlarged glands are palpable. The ulcer is now undergoing radon treatment with gold seeds.

Two pieces of skin have been examined microscopically:—

(1) Skin of back of hand. Report: Thickening of epidermis, great keratosis and chronic inflammation of the dermis. (2) Skin of right arm at site of flushed area. Report: Area of dense hypertrophic scarring of dermis with lymphocyte and plasma-celled infiltration; four separate small areas of mainly basal-celled carcinoma arising from epidermis.

Discussion.—Dr. PARKES WEBER said he thought that in regard to this case it would be better to speak of "familial generalized hyperkeratosis" than of "hereditary tylosis." The term "tylosis" was chiefly used when the palms and soles were mainly or exclusively affected. The condition in the present case seemed to have been to some extent transmitted by the patient to his children, but the patient himself possibly may have been the first case in the family. Most diseases or abnormalities of the congenital-developmental class must originally have arisen *de novo*, by *mutation*, though afterwards transmitted to descendants. Hence eugenics, however useful, would never be able to keep the world absolutely free from diseases and abnormalities of the congenital-developmental class.

Dr. J. D. ROLLESTON said that some years ago he had occasion to show a case of tylosis in which there was a history of the condition in five generations.[1] He had seen three members of the family, and the lesions were confined to the palms and the soles. The synonym was keratoderma palmare et plantare hereditarium.

The condition was endemic in the island of Meleda, off the coast of Dalmatia.

Dr. ELIZABETH HUNT said she had had a case of tylosis in a woman in whom the keratoderma extended from the palms of the hands on to the dorsal surfaces, forming

[1] *Proceedings*, 1922-23, xvi, 24; and *Brit. Journ. Child. Dis.*, 1923, xx, 16 (bibliography).

constricting bands at the interphalangeal joints, and in that case the condition had existed from birth. The woman had two children, and both were absolutely free from the condition, and there was no history of such a disease in any members of her family. The present age of the woman was 36; a short time ago gangrene had begun in the terminal phalanx of the little finger, and she had now lost that phalanx.

Erosions and Ulcers of the Tongue. ? Tuberculous.—HENRY CORSI, F.R.C.S.

E. H., male, aged 23. Family and personal history of good health. Clinical examination of chest negative; a radiogram shows two calcareous deposits. Wassermann and Sigma reactions repeatedly negative. Mantoux test positive.

1922. Loss of voice to loud whisper. Larynx found to be red, swollen, and granular, with some grey areas apparently ulcerated.

1923. Piece of right vocal cord examined; found to consist of non-specific chronic inflammatory tissue. Voice improved gradually, but has remained husky ever since.

1930. Left side, and, later, under surface of tongue, became affected. Left side has healed leaving slight scarring. Right side is now affected. This side and the under surface now show erosions, fissures, and ulcers, some with œdematous flap-like borders. The patient thinks the lesions migrate, and our observation over twelve months seems rather to confirm this opinion. There is no induration; the tongue moves freely; there is some enlargement of the submaxillary glands but this is not marked. The condition is painless.

A year ago four injections of novarsenobillon were given, and the patient became worse. Then for eight months he had general irradiation with the carbon arc, and tincture of iodine by mouth. At first he improved, but at the end of nine months the condition on the whole was no better.

On January 1, 1932, sanocrysin injections were commenced; he has improved a good deal during the last three weeks.

A section taken a year ago showed chronic inflammatory tissue with a few giant cells present.

Apart from tuberculous ulcers in phthisical subjects, only a very few cases of tuberculous glossitis have been recorded. The objective appearances in this case correspond with some previously described, but usually the ulcers have been painful.

Discussion.—Dr. J. D. ROLLESTON asked whether Dr. Corsi had considered the advisability of cutting the patient off his smoking. This was the second case of the kind he had recently seen at the Society, the other having been shown at the Clinical Section, and that was undoubtedly tuberculous ulceration of the tongue. That patient had said that life would not be worth living without smoking. The present patient's allowance amounted to five cigarettes a day; and the speaker thought that even such a small quantity would suffice to cause mechanical, chemical and caloric irritation of the lesions.

The PRESIDENT said he was not clear as to Dr. Corsi's meaning when he spoke of tuberculous glossitis as distinguished from tuberculous ulcer of the tongue. He (the President) was familiar with the type of painful ulcer which occurred in phthisis; but what he understood to be meant by "tuberculous glossitis" was an interstitial glossitis closely simulating syphilitic gumma of the tongue.

Dr. CORSI (in reply) said that originally i.e., one or two years ago, this man smoked from twenty to twenty-five cigarettes a day, and had reduced the quantity to five daily. He, Dr. Corsi, would now try to persuade him to cease smoking altogether.

He admitted that in speaking of glossitis he had not in mind anything but an affected tongue. In his reading of the literature of the subject he had not encountered a description under "glossitis" of a deep indurated variety, as seen in syphilis; the descriptions were of superficial ulcerations and erosions, closely resembling the appearance in this case.

Benign Lymphogranulomatosis.—GODFREY W. BAMBER, M.D.

Mary K., aged 22, single.

History.—About a year ago nodules developed on the knuckles, and, later, spots appeared on the forearms, and, quite recently, on the sides of the neck. A few days before admission a painful swelling developed in the left knee-joint.

Family history.—Parents dead. No tuberculosis known in family.

On examination.—Raised purple nodules, not involving the epidermis, on the backs of the proximal metacarpal joints. In the pulps of the thumbs and fingers were similar sharply-defined nodules, some of which were in the subcutaneous tissue. Small purple infiltrated areas, not raised above the skin, scattered over backs of fingers and hands. On the forearms scattered pinhead to lentil-sized papules, varying in colour from yellow to dull red. Large raised purplish-red plaques on the elbows. Papules similar to those on the forearms, but brighter in colour over the upper parts of the sides of the neck.

The left knee was swollen, pale, and tender, with thickening of the synovial membrane. ? slight effusion. Temperature 101° F. Palpable thickening of synovial membrane of right elbow-joint, and of either bursa or tendon sheath on back of left wrist. No history of acute swelling of either of these.

Investigations.—Wassermann reaction negative. Mantoux reaction negative on second, positive on fifth day.

Blood-count.—R.B.C. 3,800,000; Hb. 74%; C.I. 0·96; W.B.C. 6,000; polys. 46%; large monos. 3%; eosinos. 1%; lymphos. 50%.

Radiological reports.—Chest: hilum, enlarged glands; no evidence of active tuberculous infection otherwise. Hands: wrist-joints suggest chronic arthritis, and the terminal phalanges appear to show small—? gouty—deposits.

Report on microscopical section.—Low power: Sharply circumscribed infiltrate occupying a superficial portion of the cutis. Overlying epidermis has been lost. The neighbouring epidermis on one side shows considerable hyperkeratosis. The cutis below the infiltrate appears normal. The infiltrate consists of cells which do not stain very deeply, some of them being apparently giant cells.

High power: The infiltrate is extremely rich in giant cells of the tuberculous type. The other cells appear to be mainly fibroblasts and young connective-tissue cells with a few lymphocytes. Epithelioid cells and plasma cells are not apparent, at any rate with this stain. The epidermis shows many vacuolated cells as well as hyperkeratosis.

Discussion.—Dr. W. N. GOLDSMITH said that, because of the clinical character, the positive tuberculin reaction, and the histology, it was difficult to consider this case as an example of sarcoid. The histology was quite peculiar; he (the speaker) had never seen a similar picture. The material taken for biopsy was a tiny superficial, warty lesion. Microscopically it revealed a very compact circumscribed infiltrate consisting of numerous large giant-cells and fibroblasts mixed together, giant-cells pervading the whole infiltrate. He did not think that occurred in any phase of a typical sarcoid. Such a giant-cell and fibroblastic reaction must represent a late phase in any inflammation and as the biopsy was taken from a tiny lesion it seemed that these did not grow into the larger ones. The patient showed all gradations between tiny, warty lesions indistinguishable from juvenile flat warts and large subcutaneous nodules, some of which, for example, in the finger pulps, were quite free from overlying skin. It was, of course, possible that there was an ætiological relationship between this and true sarcoid.

The PRESIDENT said that this case reminded him, on clinical grounds, of one which he had shown before the Section in 1920,[1] the patient having previously been shown by Dr. Stowers in 1919, and by Dr. Corbett in 1915. That case had granulomatous lesions too, but distributed over the elbows and the backs of the fingers, suggesting the distribution of xanthoma, a feature to which attention was directed at the time, indeed, Dr. Adamson then

1 *Proceedings*, 1920, xiii (Sect. Derm. 63), A. M. H. Gray: "Case for diagnosis. ? Cutaneous Sarcoid of Boeck."

suggested that it might be anomalous xanthoma. From that point of view sections were cut, but there was no trace of xanthoma histologically. Also, in his own case the eruption had begun similarly as pin-head sized lesions. Another similarity was that the bursæ and synovial membranes were very much affected, more in his own case than in this. In his case there were huge bursæ round the elbows and wrists, and the whole of the upper part of front of the trunk and a good deal of the back of the trunk was covered by semi-translucent brownish lesions about the size of a large pea. He had labelled it as a sarcoid. It had differed from Dr. Bamber's in the histology. The condition had at first sight looked not unlike xanthoma; it was full of spongy cells, which did not stain with Sudan iii, surrounding masses of giant cells. There was little fibroblastic reaction.

He agreed that the histology in the present case appeared to be almost unique, but before coming to a conclusion it would be wise to examine one of the larger lesions.

Dr. BAMBER, in reply, said that the patient was reported to have had a negative tuberculin reaction on the second day. On the fifth day when he, Dr. Bamber, saw her, the reaction was positive. Some of the other cases might be delayed positives. This girl had been under treatment with intravenous injections of sodium morrhuate for three weeks, and there were now signs of improvement, especially on the forearms.

Guttate Scleroderma.—G. B. DOWLING, M.D.

This is an unusually extensive case of white-spot disease in a woman aged 59. It has been present for seven years, and there have been no associated symptoms except slight irritation. The neck, chest, abdomen and thighs are thickly studded with small, white mother-of-pearl spots, while practically the whole of the rest of the skin is hyperpigmented.

Recently an irritating superficial scaly dermatitis appeared on the upper arms and chest, but this has responded quite well to simple local treatment.

The diagnosis of atrophic lichen planus is, I think, excluded by the absolute uniformity of the mother-of-pearl lesions, and by the complete absence of any lesions resembling lichen planus.

The PRESIDENT said he thought that this type of case ought to be put into a category of its own. There was a peculiar scaliness and follicular hyperkeratosis, which was sometimes seen affecting large areas of the body, and not always in the small spot-like form seen in the present case. The cases differed in that way from the simpler form of white-spot disease, guttate scleroderma.

An Unusual Form of Erythema Multiforme Centrifugum Perstans. Case for Diagnosis.—H. W. BARBER, M.B.

H. M., aged 49, postman.

The eruption began three and a half years ago from a bruise on the left shin caused by pressure from kneeling in his van. It formed a "blood-blister." The rash appeared first around the blister and spread up to the groins and in both legs: then all over his body.

Description of eruption.—The elementary lesion is a typical disc-like papule of erythema multiforme with a central dried serous crust, representing, no doubt, a dried vesicle. These lesions tend to spread peripherally, producing circinate figures, many of which coalesce and form large composite patches. The extreme periphery of the circinate lesions is composed of an œdematous erythema characteristic of erythema multiforme; just behind this is a zone of dried crust corresponding to the central crust of the elementary lesion. The crusting may form large sheets, which eventually exfoliate, leaving pigmentation to mark the site of areas formerly affected. Some of the elementary erythema multiforme lesions are exceedingly minute—practically pin-point. Both legs are œdematous, particularly the left, which has been affected for a year: the œdema is apparently due to lymphangitis. Intradermal tests for

Streptococcus hæmolyticus, *Streptococcus viridans*, staphylococcus and tuberculin, all negative.

I think the case corresponds to that shown by Dr. Knowsley Sibley at the last meeting.

Report on microscopical section.—The dermis: The vessels of the papillæ and subpapillary zone are dilated and there is active diapedesis of leucocytes, many of which can be seen traversing the epidermis, being eventually exfoliated in the serous crust.

The epidermis: In parts there is well-marked spongiosis, the Malpighian layer appearing œdematous and the prickle-cells being swollen, ill-defined, and poorly stained. The crust is seen to be composed of parakeratotic horny cells, dried serum, and included clumps of leucocytes. At one point in the section can be seen an actual blister, containing red blood-corpuscles and lying between the epidermis and an overlying crust.

Post-Traumatic Alopecia Areata.—H. W. BARBER, M.B.

Mrs. M. C., aged 46.

History.—On November 26, 1931, she was knocked down by a tradesman's car in the street. As a result, the scalp was cut deeply from the forehead at a point about one inch from the margin of the hair backwards over the right frontal region for a distance of about four inches. The accident caused considerable shock. The scalp-wound was stitched, and healed well. On about the eighth day after the injury the hair began to fall out over the right frontal and temporal regions. For a while there was severe pain over this region with hyperæsthesia to touch.

When seen by me, January 4, 1932, there was a scar, corresponding to the scalp-wound, with loss of hair over the right frontal and temporal regions extending almost to the midline and backwards to a point one inch behind the right pinna. Two small fresh areas of alopecia had recently appeared near the midline. A large part of the affected area was completely bald. Numerous typical exclamation-mark hairs were present, and under the microscope showed the characteristic atrophy and depigmentation of the proximal portions, with "clubbing" and hyperpigmentation of the distal ends. Some new downy hair was beginning to appear in places.

This is clearly a genuine case of post-traumatic alopecia areata. Lévy-Franckel and Juster in a recent article (*Annales de Derm. et de Syph.*, vii^{e}, Série II, No. 10, 1931, 1074) have given an interesting review of cases of alopecia from trauma and from shock. The cases may briefly be classified as follows:—

(1) *Traumatic alopecia areata.*—In these cases, according to Montier and Legrain (*Annales de Derm. et de Syph.*, 1928, iv, 268), the alopecia always follows injuries to the face or cranium, and the interval between the injury and the onset of the alopecia is not longer than two months. My case comes into this category. But according to Lévy-Franckel and Juster, there is another group of traumatic cases in which the alopecia is consecutive to severe injuries to the limbs. In these the interval between the injury and the alopecia is a matter of years. In the majority of cases the injury to the limbs is very severe, with fractures and extensive involvement of the muscles, nerves and vessels, and leaves local symptoms of sympathetic-nerve disturbance—hyperidrosis, glossy skin, causalgia—and sometimes of a general endocrine-sympathetic dysfunction. The alopecia in these cases is ascribed to an ascending neuritis of slow extension, which eventually reaches the sympathetic nerve-centres in the cord that are in relationship with the capillary circulation in the scalp.

(2) *Alopecia areata from shock.*—In these cases the incubation period between the shock and the fall of hair is very short—two or three days. The loss of hair is, as a rule, rapid and extensive involving the scalp and other hairy parts—defluvium capillorum. There is a general disturbance of the endocrine-sympathetic system as in Graves' disease, and no doubt many of these patients are of the hyperthyroidic type with a raised basal metabolism.

Lévy-Franckel and Juster, in fact, recognize two groups of cases in alopecia areata:

(1) endocrine-sympathetic with a modified basal metabolism, (2) vasculo-sympathetic, with a normal basal metabolism. The traumatic cases belong to the latter group; the "shock" cases to the former.

Seborrhœic Verrucæ and Multiple Basal-celled Epitheliomata.—KNOWSLEY SIBLEY, M.D.[1] (Further histological report and comment by Dr. I. K. MUENDE).

This case was shown as one of Multiple Benign Epithelioma of Little, in which the lesions are seen to take their origin from verrucæ seniles ("seborrhœic warts"). In a microscopic section rodent cells can be seen arising at several points from the lower poles of the rete pegs of a verruca. The rodent tissue appears to be growing intradermally at the expense of the warty tissue. The section confirms the opinion that the rodent is growing from the wart and not invading it from without as was suggested at the last meeting.

[1] Case shown at the Meeting held December 17, 1931; see *Proceedings*, 1932, xxv, 670, Sect. Derm. 28.